or a physiologically acceptable salt thereof for the reduction ~~of the risk~~ **in the level of iron burden in the heart** ~~of heart disease~~ in **heavily transfused** patients ~~having~~ **experiencing** iron overload **of the heart**, ~~such as in thalassemia or the like comprising an effective amount of deferiprone or a physiologically acceptable salt thereof~~ **said therapeutic amount being** sufficient to ~~treat~~ **reduce** iron **burden in the heart and the resulting iron** induced cardiac disease ~~normally associated with iron overload~~.

11. (currently amended) A method of preventing ~~the risk of~~ heart disease in **heavily transfused** patients ~~having~~ **risking** iron overload **of the heart**, ~~such as in thalassemia or the like~~ comprising the administration of a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to ~~treat~~ **prevent** iron induced cardiac disease ~~normally associated with iron overload~~.

12. (currently amended) A method of stabilizing ~~the risk of~~ heart disease in **heavily transfused** patients having iron overload, ~~such as in thalassemia or the like~~ comprising the administration of a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to treat iron **burden in the heart normally associated with** induced cardiac disease ~~normally associated with iron overload~~.

13. (currently amended) A method of reducing ~~the risk of~~ **the iron burden in the heart associated with** heart disease in **heavily transfused** patients having iron overload, ~~such as in thalassemia or the like~~ comprising the administration of a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to ~~treat~~ **reduce the iron burden of the heart normally associated with** iron induced cardiac disease ~~normally associated with iron overload~~.

18. (currently amended) A **pharmaceutical composition for iron induced cardiac disease comprising a** therapeutically effective amount of **the iron chelator** deferiprone or physiologically acceptable salt thereof for the prevention, treatment, or reversal of heart disease in **heavily transfused** patients ~~having~~ **risking or experiencing** an iron overload condition of the heart**,** ~~comprising an effective amount of deferiprone or a physiologically acceptable salt thereof~~ **said therapeutic amount being sufficient** to ~~preferentially~~ reduce the iron stores in the heart **and** in ~~comparison~~ **preference** to the iron stores in less critical organs/tissue in the body.

22. (currently amended) A method of treating~~/preventing/or reversing~~ heart disease in a **heavily transfused** patient having an iron overload condition of the heart comprising administering to the patient a therapeutically effective amount of deferiprone, or a physiologically acceptable salt thereof

in order to ~~preferentially~~ reduce the iron stores in the heart in ~~comparison~~ **preference** to less critical organs/tissue in the body.

23. (currently amended) A method of ~~treating/~~preventing~~/or reversing~~ heart disease in **heavily transfused** patients having an iron overload condition of the heart comprising administering to the patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof to ~~preferentially reduce~~ **chelate** the iron stores in the heart in ~~comparison~~ **preference** to the iron stores in less critical organs/tissue in the body.

24. (currently amended) A method of ~~treating/preventing/or~~ reversing heart disease in **heavily transfused** patients having an iron overload condition of the heart comprising administering to the patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof to ~~preferentially~~ reduce the iron stores in the heart in ~~comparison~~ **preference** to the iron stores in less critical organs/tissue in the body.

25. (currently amended) A method of treatment, prevention, or reversal of heart disease in a **heavily transfused** patient having an iron overload condition of the heart comprising administering to the patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof for the direct ~~preferential~~ reduction/removal of ~~iron (for example~~ intracellular iron~~)~~ stores in the heart.

26. (currently amended) A method to prevent/treat/reverse the occurrence of iron-induced cardiac disease in **heavily transfused** patients with an iron overload condition ~~such as thalassemia or the like~~, comprising administering to said patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof, wherein deferiprone's efficacy is cardio preferential when compared with its ability to lower total iron stores in the body.

30. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising the~~ **wherein** ~~active ingredient~~ deferiprone or a physiologically acceptable salt thereof **is administered orally** for preventing the risk of heart disease in patients having iron overload.

31. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising the~~ **wherein** ~~active ingredient~~ deferiprone or a physiologically acceptable salt thereof **is administered orally** for stabilizing the risk of heart disease in patients having iron overload.

32. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising the~~ **wherein** ~~active ingredient~~ deferiprone or a physiologically acceptable salt thereof **is administered orally** for reducing the risk of heart disease in patients having iron overload.

33. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising an oral dosage form of~~ **wherein** deferiprone or a physiologically acceptable salt thereof **is present is an oral dosage form** with other excipients.

35. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising daily~~ **wherein the** administration **frequency to the patient** of an amount of deferiprone or a physiologically acceptable salt thereof **is daily and** substantially in the range of up to 150mg~~/kg to the patient.~~ **per kilogram of body weight.**

37. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising~~ **wherein the** administration **frequency to the patient** of a ~~daily~~ dosage amount of deferiprone or a physiologically acceptable salt thereof **is daily and** substantially in the range of up to 125 mg~~/kg to the patient.~~ **per kilogram of body weight.**

39. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising~~ **wherein the** administration **frequency to the patient** of a ~~daily~~ dosage amount of deferiprone or a physiologically acceptable salt thereof **is daily and** substantially in the range of 25mg~~/kg~~ to 75mg~~/kg to the patient.~~ **per kilogram of body weight.**

41. (original) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 wherein deferiprone is administered in a manner selected from the group of intravenously, transdermally, rectally, orally, bucally, or aurally.

43. (original) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 wherein deferiprone is administered orally.

45. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 wherein ~~the dosage form~~ **deferiprone or a physiologically acceptable salt thereof** is **in** a sustained release formulation.

47. (original) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 wherein deferiprone has a cardio preferred/selective function when compared to desferrioxamine or other alternative chelating agents utilized in patients suffering iron overload.

49. (original) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 wherein deferiprone is administered in addition to desferrioxamine.

51. (cancelled)

52. (cancelled)

53. (cancelled)

54. (cancelled)

55. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 ~~further comprising~~ **wherein said composition is administered to the patient** daily ~~administration of an amount of deferiprone or a physiologically acceptable salt thereof~~ **and** substantially in the range of up to 150mg~~/kg to the patient.~~ **per kilogram of body weight.**

56. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 ~~further comprising administration of a~~ **wherein said composition is administered to the patient** daily ~~dosage amount of deferiprone or a physiologically acceptable salt thereof~~ **and** substantially in the range of up to 125 mg~~/kg to the patient.~~ **per kilogram of body weight.**

57. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 ~~further comprising administration of a~~ **wherein said composition is administered to the patient** daily ~~dosage amount of deferiprone or a physiologically acceptable salt thereof~~ **and** substantially in the range of 25mg~~/kg~~ to 75mg~~/kg to the patient.~~ **per kilogram of body weight.**

58. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 wherein ~~deferiprone~~ **the composition** is administered in a manner selected from the group of intravenously, transdermally, rectally, orally, bucally, or aurally.

59. (cancelled)

60. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 wherein the ~~dosage form~~ **composition** is **in** a sustained release formulation.

61. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 wherein ~~deferiprone~~ **said composition** has a cardio preferred/selective function when compared to desferrioxamine or other alternative chelating agents utilized in patients suffering iron overload.

62. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 wherein ~~deferiprone~~ **the composition** is administered in addition to desferrioxamine.

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REMARKS

The Examiner states that the Abstract of the disclosure is objected to because it does not appear on a separate page without extraneous subject matter present. A revised abstract on a separate page is attached to this response for the Examiner's consideration.

Claims 1, 2, 8-13, 18, 25, 30-32, 33, 35, 37, 39, 45, 54, 55-59, 60 and 62 now stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims therefore have been revised consistent with the Examiner's suggestions on pages 3 and 4 of his report and full reconsideration is requested.

With respect to claims 55, 56 and 57 applicants have amended these claims to more specifically identify that the composition is administered in the specified amount per kilogram of body weight of the patient. This approach further follows a well known convention present in the patent and peer reviewed literatures, for example in Hoffbrand cited by the Examiner. Full reconsideration is therefore requested.

Applicant will now provide the Examiner with further general discussion and perspective information. In conditions of iron overload, such as those with the genetic blood disorder, thalassemia major, patients develop iron-induced organ damage as a result of chronic and frequent blood transfusions. Blood transfusions are necessary to sustain life because of the inability of the body to maintain an adequate hemoglobin level due to its defective formation and rapid degradation. However, the frequent blood transfusions (every 2-3 weeks), result in massive iron loading in the body, with a non-homogeneous distribution of the iron among the tissues. Typically, the liver will accumulate the most iron and various other organs, glands and other tissues much less. Animal studies suggest that the ratio of liver iron to heart iron per gram of tissue is approximately 10:1. Yet, the primary cause of death in patients with thalassemia is due to iron-induced heart disease, not liver disease, with about 70% of the patients dying from iron-induced cardiac disease.

Deferoxamine was the first iron chelator to be approved for clinical use in conditions of iron overload. The chronic use of deferoxamine resulted in a substantive decrease in the total body burden of iron and a decrease in morbidity and a prolongation of life. The use of deferoxamine was reported to facilitate not only the removal of iron from the body, but also the survival without iron-induced cardiac disease *(Olivieri NF, Nathan DG, MacMillan JH, et al. "Survival in medically treated patients with homozygous -thalassemia", N Engl J Med 1994;331:574-578)*.

One of the first well-described and detailed studies on the use of deferiprone in thalassemia patients, spanning a period of several years, was published in the New England Journal of Medicine in April 1995 *(Olivieri NF, et al "Iron-chelation therapy with oral deferiprone in patients with thalassemia major", 332(14):918-22).* The article reported deferiprone reduced the total body burden of iron, as judged by liver iron concentrations and serum ferritin concentrations. The response of the patients led the author to conclude ***(precise wording: Our data provide direct evidence of the efficacy of deferiprone for the treatment of iron overload in patients with thalassemia major. Deferiprone decreases body iron concentrations and maintains them at levels below those associated with the complications of iron overload).*** Although the use of deferiprone seemed to be a promising alternative to deferoxamine to lower total body burden of iron, there was no evidence of a unique cardio protective effect. In fact, an accompanying editorial by Dr. David Nathan made it clear that, while the data were encouraging, the lack of evidence that deferiprone had any ability to remove iron from the heart and thus increase survival, raised questions as to its utility: *"Not enough is known about the pharmacologic properties of deferiprone. Will the low levels of drug that remain in the plasma continue to chelate free iron and thereby protect heart-muscle membranes, or will the small but highly toxic pool of free iron remain or return to high levels between doses to do its damage? Over time, will the drug's ability to be absorbed prove to be a two-edged sword because it can also permeate the cell membranes of vital organs such as the kidney, with toxic effects?"* ***(Nathan D. G. An orally active iron chelator. N.Engl.J.Med. 332 (14):953-954, 1995).***

Subsequently, several articles appeared in the medical literature indicating that the use of deferiprone was less effective than the use of the other iron chelator, deferoxamine, in removing iron from the body. This was assessed primarily by liver iron concentrations and, in some cases, by serum ferritin concentrations over time. Thus, it was expected that, on the basis of the ability to reduce the iron body burden alone, one would reasonably predict lesser benefit from deferiprone in terms of survival related to iron-induced cardiac disease. That is, if any potential cardio-protective effect was solely related to the ability of an iron chelator to remove iron from the body, as was understood to be the case for deferoxamine, then deferiprone should have less effect than deferoxamine as a cardio-protectant.

In 1998 ***(Olivieri N. F., Butany J., Templeton D. M., and Brittenham G. M. Cardiac Failure and Myocardial Fibrosis in a patient with Thallassemia Major (TM) Treated with Long-Tem Deferiprone. Blood 1998; 92:532a.)*** this same author published a report at the annual meeting of ASH, that she believed deferiprone had been responsible for the decline in the cardiac function of a patient and that this decline was associated with myocardial fibrosis as well. Clearly, the only evidence that had been in the literature at that time, suggesting, if at all, that there might be some

benefit of deferiprone affecting the heart, was clearly rejected by the very person who published that information and in 1998 she had come to the conclusion that the opposite was the case.

The data that provided the evidence of the preferential cardio-protection of deferiprone was the work that Applicant conducted in Torino, which formed the basis for this application, to evaluate the response of all patients in the same center treated by the same clinical team in the same manner with the exception that some patients received deferiprone and some deferoxamine. That study revealed that there was a preferential effect in the deferiprone-treated patients in protecting the heart, both from iron-induced cardiac disease as well as survival, that could not be explained by the removal of iron from the body alone. That is, the patients receiving deferiprone did not excrete more iron from the body than did patients receiving deferoxamine, yet clearly there was a preferential cardiac benefit in deferiprone-treated patients. These data clearly demonstrate that there was a direct benefit to the heart obtained from using deferiprone that was not simply due to the removal of iron from the body, and was not predictable based on the potency of deferiprone compared to deferoxamine.

It has been reported that increased iron overload results in an increase in iron-induced cardiac damage. It has also been reported that the removal of iron from the body is likely to decrease that risk. Thus one reasonably should conclude that an iron chelating agent which induces a greater elimination of iron from the body, should also exhibit a greater decline in the risk of iron-induced cardiac damage. That, however, is not the case with deferiprone. The decline in body iron burden with this drug compared to deferoxamine, as evidenced by changes in liver iron concentrations, the most extensive site of iron storage in the body, would predict that deferoxamine would have had a greater cardio-protective effect than deferiprone. Since these data from the Torino study demonstrate exactly the opposite effect, one can only conclude there is a preferential effect of deferiprone, not predicted by the removal of iron from the body alone. Thus the discovery is unpredicted from the literature.

Claims 8, 9, 10, 18, 51-59 now stand rejected under 35 U.S.C. 102(b) as being allegedly anticipated by any one of Olivieri et al., Hoffbrand et al. (Examiner cit. Ref. "U") or Hoffbrand et al. (Examiner cit. Ref. "V") who each purport to teach as alleged by the Examiner, an effective therapeutic amount of deferiprone at a dosage of 75mg/kg/day.

Claims 1, 2, 8-13, 18, 22-26, 30-33, 35, 37, 39, 41, 43, 45, 47, 49 and 51-62 now stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Lai (US Patent No. 5,922,761) who purports to teach methods for the reduction of free iron levels in a subject in which a dithiocarbamate containing composition iron chelator is administered, but not deferiprone.

Before commencing any rebuttal with reference to any alleged prior art issues the Examiner is respectfully directed towards the following exerpted case law from which Applicant will draw liberally.

ANTICIPATION

The following excerpts of U.S. case law represent Applicant's understanding of the test for novelty and obviousness.

In Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986) ("It is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention, and that such a determination is one of fact.").

In re Donohue, 766 F.2d 531, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985) ("an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice, or device.").

In Atlas Powder Co. v. E.I. du Pont De Nemours & Co., 750 F.2d 1569, 1574, 224 U.S.P.Q. 209, 411 (Fed. Cir. 1984) ("exclusion of a claimed element from a prior art reference is enough to negate anticipation by that reference").

In Tights, Inc. v. Acme-McCrary Corp., 541, F.2d 1047, 191 U.S.P.Q. 305 (4th Cir. 1976); Saf-Gard Prods., Inc. v. Service Parts, Inc., 532 F.2d 1266, 190 U.S.P.Q. 455 (9th Cir. 1976); Shanklin Corp. v. Springfield Photo Mount Co., 521 F.2d 609, 187 U.S.P.Q. 129 (1st Cir. 1975) ("To anticipate under section 102, a prior art reference must disclose all the elements of the claimed invention or their equivalents functioning in essentially the same way.").

In re Beno (1985) 768 F.2d 1340, 226 U.S.P.Q. 683 (Fed. Cir. 1985) a prior art patent or published application is a reference only for that which it teaches.

In re Sun, 31 USPQ 2d 1451, 1453 (Fed. Cir. 1993) (unpublished)

Under section 102(b), anticipation requires that the prior art reference disclose, either expressly or under the principles of inherency, every limitation of the claim. . . .

But to be prior art under section 102(b), a reference must be enabling. . . . That is, it must put the claimed invention in the hand of one skilled in the art. . . . The examiner bears the burden of presenting at least a prima facie case of anticipation.
Helifix Ltd. v. Blok-Lok, Ltd., 54 USPQ 2d 1299, 1304 (Fed. Cir. 2000)

"[E]ven if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling." *Donohoe*, 766 F.2d at 533, 226 USPQ at 621.

In re Wilder, 166 USPQ 545, 548 (C.C.P.A. 1970)

Simply stated, a prior publication or patent description will be considered as anticipatory when its disclosure is at once specific and enabling with regard to the particular subject matter at issue. . . . However, such disclosure may yet be held not to legally anticipate the claimed subject matter if it is found not to be sufficiently enabling, in other words, if it does not place the subject matter of the claims within "the possession of the public."

Ciba-Geigy Corp. v. Alza Corp., 37 USPQ 2d 1337, 1341 n.3 (Fed. Cir. 1995) (unpublished)

An anticipatory reference must be enabling, *see Akzo N.V. v. United States Int'l Trade Comm'n*, 808 F.2d 1471, 1479, 1 U.S.P.Q.2D (BNA) 1241, 1245 (Fed. Cir. 1986), *cert. denied*, 482 U.S. 909, 96 L. Ed. 2d 382, 107 S. Ct. 2490 (1987), so as to place one of ordinary skill in possession of the claimed invention. *In re Spada*, 911 F.2d 705, 708, 15 U.S.P.Q.2D (BNA) 1655, 1657 (Fed. Cir. 1990); *see Seymour v. Osborne*, 78 U.S. 516, 555, 20 L. Ed. 33 (1870) ("The knowledge supposed to be derived from the publication must be sufficient to enable those skilled in the art or science to understand the nature and operation of the invention.").

OBVIOUSNESS

The traditional test enunciated in Graham vs. John Deere Company 383 U.S. 1, 148 U.S.P.Q. 459 1966, for Section 103 nonobviousness requires the fact finder to make several determinations. The test provides that the scope and content of the prior art be determined, the differences between the prior art and the claims at issue be ascertained, and the level of ordinary skill in the pertinent art be resolved. Thus, the patentability of the claims at hand must stem from the fact that the specific combination of the claimed elements was not disclosed in the prior art and the additional allegation that the specific combination of claimed elements was nonobvious to one of ordinary skill in the art.

Clearly, the prior art does not suggest or provide any reason or motivation to make such a modification as purported by the Examiner. With reference to In Re: Regal, 526 F. 2d 1399, 1403 n. 6, 188 USPQ 136, 139 n. 6 (CCPA 1975).

> "There must be some logical reason apparent from positive, concrete evidence of record which justifies a combination of primary and secondary references".

In Re: Geiger, 815 F. 2d 686, 688, 2 USPQ 2d 1276, 1278 (Fed. Cir. 1987) (obviousness can not be established by combining pieces of prior art absence some "teachings, suggestion, or incentive supporting the combination"): In Re: Cho. 813 F. 2d 378, 382, 1 USPQ 2d 1662, 1664 (Fed. Cir. 1987)("discussing the Board's holding that the artisan would have been motivated to combine the references").

Therefore, it Applicant's view there is no evidence of motivation in the prior art, either within the references themselves, or knowledge generally available to one of ordinary skill in the art, to make the purported changes suggested by the Examiner to arrive at the claimed subject matter.

Respectfully, the Examiner is creating a 20/20 hindsight reconstruction using Applicant's invention as a blue print to allegedly find elements of Applicant's combination in the prior art. This is not permissible as set out below.

In re Oetiker, 24 USPQ 2d 1443, 1446 (Fed. Cir. 1992)

The combination of elements from non-analogous sources, in a manner that reconstructs the applicant's invention only with the benefit of hindsight, is insufficient to present a prima facie case of obviousness. **There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the combination.** (emphasis added)That knowledge can not come from the applicant's invention itself.

ATD Corporation v. Lydall, Inc., 48 USPQ 2d 1321, 1329 (Fed. Cir. 1998)

Determination of obviousness can not be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention. **There must be a teaching or suggestion within the prior art, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources of information, to select particular elements, and to combine them in the way they were combined by the inventor.** (emphasis added)

In Re: Fritch, 23 U.S.P.Q. 2d 1780 (Fed. Cir. 1992)

"Wilson and Hendrix fail to suggest any motivation for, or desirability of, the changes espoused by the Examiner and endorsed by the Board. Here, the Examiner relied upon hindsight to arrive at the determination of obviousness. **It is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art so that the claimed invention is rendered obvious** (emphasis added). The court has previously stated that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."

Applicant's will now address the anticipation rejections by reviewing the alleged prior art documents and specifically what each of Olivieri, Hoffbrand (Ref. "U") or Hoffbrand (Ref. "V") teach.

Referring to *Olivieri, document U or document V*, the Examiner respectively is advised that reaching general conclusions to support an alleged position of anticipation is insufficient when the overall teachings of the document are clear, and sadly lacking.

Reference is now made to *Olivieri, et al "Reduction of tissue iron stores and normalization of serum ferritin during treatment with the oral iron chelator deferiprone in thalassemia intermedia", 1992 in Blood, Vol. 79*. The Examiner is not, respectfully, looking at the overall teachings thereof. The reference makes some general comments with regard to slight improvements over a nine month period in a patient with thalassemia intermedia, and on page 2744 at the bottom thereof, there is discussion that before L1 therapy there was an abnormal resting electrocardiogram and the various heart functions, and then after nine months of L1 therapy a comparison was made to those rates. It is stated that the abnormalities of the right ventricular dilatation and abnormalities in diastolic function **did not change during L1 therapy** except for a slight improvement in atrial contribution. This reference therefore suggests that it would be worthwhile to pursue, in spite of the complications inferred in the paper, the warranted use of L1 as a therapeutic option in patients with thalassemia intermedia having iron over-load. There is only discussion of mild improvement in the heart performance, but there is no discussion of the unexpected advantages pointed out in Applicant's disclosure that deferiprone is 4 times more effective than deferoxamine in managing cardiac problems in patients with thalassemia. Please note that the author of this reference in further study as supported in the prior discussion in, the reference from 1998 to Olivieri, et al changed her position with respect to the efficacy of deferiprone, in that it *"May not provide adequate sustained control of body iron in a substantial proportion of Cooley's anemia patients."*

The question therefore remains, what therefore would be the state of the art; the submissions in 1992 reference or those in the 1998 reference by the same leading author.

Referring again to Olivieri it is clear that Olivieri particularly refers to a reduction in tissue iron stores and normalization of serum ferritin concentrations. The reference teaches that there was a dramatic improvement in signal intensity of the liver with respect to MRI results but only mild improvement for the heart. The report therefore provides "the first report of normalization of serum ferritin concentration in parallel with demonstrated reduction in tissue iron stores as a result of treatment with L1". Clearly Olivieri refers to a reduction in tissue or body iron in serum ferritin levels and specifically the liver for only one individual and yet pointing to only mild improvement for the heart.

Referring now to document "U" namely Hoffbrand, 1997, clearly the Examiner has read more into the teachings of Hoffbrand than that which is present. The Examiner erroneously assumes that reducing body iron stores generally will reduce those in the heart. Hoffbrand clearly states that deferiprone is capable of maintaining body iron stores at safe levels and that trials had been conducted to increase the dosages of deferiprone in order to achieve lower body iron burden in these patients. Clearly therefore Hoffbrand in 1997 did not appreciate the fact that deferiprone in fact would not necessarily decrease body iron burden in patients and even if it did there was no expectation that this might in fact relate to significant improvement in cardiac iron burden. In fact in document "U" Hoffbrand concludes that patients with cardiomyopathy due to iron overload should be given intravenous DFX rather than deferiprone. Hoffbrand therefore clearly points towards desferroxamine as opposed to deferiprone in the teachings of document "U" for patients experiencing cardiac problems.

Referring now to document "V" also to Hoffbrand, again there is a discussion referring to total iron loading in the body. Hoffbrand focuses on the serum ferritin levels and concludes that there is no overall significant change therein or in urine iron excretion. Hoffbrand therefore says that the results therefore imply that there is no overall change in iron stores with respect to the iron chelator deferiprone. He however makes no conclusion with respect to the heart in this regard but merely states that the iron status is maintained.

Neither reference "U" or "V" therefore can be considered as anticipating the present claim set since Hoffbrand does not even consider the impact on the heart nor the cardio selective and preferred and protective effects of deferiprone. He does not even recognize this fact although he considers body iron is maintained. No where within either reference nor in Olivieri is there discussed the fact that in spite of the fact that serum ferritin levels may not have changed, or that the overall body iron has

changed nor that serum ferritin levels might have been maintained, nor the urinary iron excretion is significantly different, that deferiprone works in a different way than desferroxamine and that these body iron level indicators do not impact upon the cardio preferential action of deferiprone as Applicant has discovered.

In order for a reference to anticipate it has to meet each and every element of the amended claims that is say each limitation of the claim must be found in a single reference and functioning in essentially the same way.

Clearly however none of Olivieri, Hoffbrand (Ref. "U") or Hoffbrand (Ref. "V") are enabling with respect to any anticipation rejection purported by the Examiner in that they do not teach the following:

> *8. A pharmaceutical composition for iron induced cardiac disease comprising an effective therapeutic amount of the orally administered iron chelator deferiprone or a physiologically acceptable salt thereof for the prevention of heart disease in heavily transfused patients risking an iron overload condition of the heart, said therapeutic amount being sufficient to prevent further iron accumulation in the heart associated with iron induced cardiac disease.*

It is therefore suggested that none of the references refer to the therapeutic value of deferiprone with respect to preventing iron accumulation and further iron accumulation in the heart associated with iron induced cardiac disease. The limitations of for example, claim 8 as stated above are not found in any of the references of Olivieri, Hoffbrand (Ref. "U") or Hoffbrand (Ref. "V"). None of the references teach this specific combination related to an iron overload condition of the heart.

Out of an abundance of caution should the Examiner allege that documents of Olivieri, Hoffbrand (Ref. "U") or Hoffbrand (Ref. "V") might render the claims obvious to those skilled in the art applicant suggests that there is no motivation within the teachings of any of the above-mentioned three references to arrive at Applicant's claim 8 as above or any of the other rejected claims as amended above and provided in Applicant's response. The claims have sufficiently been amended namely claims 8, 9, 10, 18, and 51-59 so as to clearly distinguish over the prior art and any possible obviousness rejection the Examiner might make.

Referring to the traditional test in Graham v. John Deere Company for obviousness Applicant has determined the scope and content of the prior art and provided and set out the differences between the prior art and the claims at issue. The clear conclusion following this case therefore is that the

claims are patentable which stems from the fact that the specific combination of the claimed elements was not disclosed in either of Hoffbrand, Olivieri namely Hoffbrand (Ref. "U" or "V") and that the specific combination was nonobvious. Clearly there is no motivation from the art to arrive at Applicant's teachings set out in the amended claims set out above. Clearly the references do not teach Applicant's claims nor were the claims apparent to one skilled in the art when considering the state of the art at the date prior to Applicant's discovery.

Referring now to the Examiner's alleged 35 U.S.C. 103(a) rejections for the above-mentioned claim set over Lai (US Patent 5,922,761) respectfully Applicant fails to see the relevance of said '761 Patent referring to dithiocarbamate as a chelating agent. Clearly the Examiner has realized the difference as stated that Lai does not teach deferiprone compositions. However the Examiner states that a skilled person would consider this difference obvious and refers to the teaching of specifically column 3, line 24-34 of the '761 reference found in the background of the invention. At this particular point in the reference it is stated that:

> and related compounds are orally available iron chelators, showing promise in improving the quality of life in patients with thalassemia (see, for example, Olivieri et al., in *Drugs Today* 28(Suppl. A): 123–132 (1992)) and rheumatoid arthritis (see, for example, Vreugdenhil et al., in *Lancet* 2:1398–9 (1989)). However, the major side effects of L1 therapy include myelosuppression, fatigue, and maternal, embryo and teratogenic toxicity, which severely limits the potential clinical applications thereof (see, for example, Kontoghiorghes, in *Int. J. Hematol.* 55:27–38 (1992)).
>
> Recently, ICRF-187 has been demonstrated to be effective

Clearly the Examiner has misread the reference in trying to state that the use of dithiocarbamate based formulations and deferiprone are interchangeable. Clearly this is not the case from the '761 Patent at all and specifically Lai has stated that there is a need in the art for a new class of iron chelators that is capable of removing free iron ions from body fluids without effecting the normal cellular iron metabolism. Lai states that one normally supplements zinc in patients chelated with deferiprone. However no demonstrated understanding of the cardioprotective benefits of dithiocarbamate is taught in order to protect the heart. Most assuredly, this being the case, there is no motivation to use deferiprone in this regard from the teaching of Lai. Clearly therefore Lai does not even understand Applicant's invention or discovery with respect to the cardio preferential action of deferiprone. This teaching is not found within Lai nor within any of the other prior art of which Applicant is aware. Although one skilled in the art might be motivated to consider use of deferiprone as an iron chelator (with no admission that this is the case) as Lai has suggested it in the background

of his invention, they clearly would not understand the cardio preferential value of deferiprone for a heavily transfused patient, such as those suffering from thalassemia. Further there is no motivation within the references cited by the Examiner that teaches the use of desferroxamine and deferiprone together nor deferiprone in a sustained release formulation.

Respectfully the Examiner is creating a 20/20 hindsight reconstruction using Applicant's invention as a blueprint to allegedly find Applicant's elements in the prior art which is not permissible. See in re Oetiker and ATD Corporation v. Lydall, Inc.

Clearly therefore as set out below in claim 1:

> *A method of treating iron induced cardiac disease in a heavily transfused patient experiencing an iron overload condition of the heart, said method comprising administering to the heavily transfused patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to stabilize/reduce/iron accumulation in the heart resulting from being heavily transfused and preventing further iron accumulation in the heart normally associated with iron induced cardiac disease.*

nothing within Lai teaches the above-mentioned method. There is no motivation in Lai to do so nor would it be apparent to one skilled in the art. One skilled in the art in reading Lai would have to take a gigantic leap to arrive at Applicant's amended claim set.

Full reconsideration is respectfully requested.

However, referring to the present disclosure, Applicant has clearly statistically verified the unexpected and surprisingly profound discovery contrary to the references cited by the Examiner which may be considered as only helpful that deferiprone in spite of varying serum ferretin levels has a cardio selective and preferred chelating function when compared to desferroxamine in spite of the lack of significant differences between the two chelators in a reduction in overall iron excretion. Deferiprone appears to have a preferred or preferential effect on the heart than other organs and overall body iron. This has been definitively proven in the clinical study within the present patent application. Although the prior literature does suggest that both desferroxamine and deferiprone eliminate iron from the body, it is clear from the comparison with desferroxamine in the present application in the clinical studies that DFO's effect on the heart is secondary compared to the overall body, the liver, and possibly the blood. The data reveals that iron induced heart disease occurs even in patients who are compliant with desferroxamine and even for those who do not have high levels of total body iron as assessed by serum ferretin or liver iron concentrations. It has thus become evident

that lowering of the total body iron alone is insufficient to protect against iron induced heart damage.

Applicant had listed many references in its extensive list of references 1 through 62 in the background of the invention and stated that there are more than 250 articles in the peer reviewed literature which refer to deferiprone, and 48 of which present data on the use of deferiprone in patients with iron overload. However, in Applicant's opinion there is no literature that demonstrates that deferiprone has a greater cardio protective effect than desferroxamine or that it might have activity beyond its general ability to reduce the total body iron load, and benefit to heart function. Applicant's have discovered that the administration of effective amounts of deferiprone results in patients being at less risk of developing cardiac disease than a patient treated with desferroxamine. Deferiprone preferentially reduces the iron stores in the heart in comparison to the iron stores in less critical organ/tissue in the body. Deferiprone's efficacy is cardio preferential when compared with its ability to lower total iron stores in the body.

Applicant has proven statistically the unexpected result discussed above that deferiprone can remove iron from the iron overloaded heart to a greater extent than what would be expected from the clinical studies conducted.

This specification teaches an even greater protective effect than could be expected from overall body iron reduction alone. Clearly, there is no discussion in the prior literature with regard to the preference of deferiprone to the iron stores in the heart as set out in many of the claims with Applicant's claim set.

Clearly, therefore the afore-mentioned references do not anticipate nor render obvious any of claims 1 through 62 in spite of the Examiner's incorrect assertions. Applicant's results are contrary to the conclusion in the art. They are unexpected and surprisingly contrary to the art.

If the Examiner has any questions, he is requested to contact Neil H. Hughes at (905) 771-6414 at his convenience.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Registration No. 33,636
Agent for the Applicant

NHH/lvp
Enclosures

ABSTRACT

A method of treating iron induced cardiac disease in a patient with iron overload, such as in thalassemia or the like comprising administering to the patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to treat iron induced cardiac disease normally associated with iron overload.

1614
JFW

IN THE UNITED STATES PATENT OFFICE

In re application of	:	Apotex Inc.		
Serial No.	:	10/311,814	Our Ref.	: PC-1834033
Group Art Unit	:	1614	**CUSTOMER NO. 23607**	
Filed	:	April 4, 2004	Examiner	: Raymond J. Henley III
For	:	A New Use for Deferiprone		

REQUEST FOR EXTENSION OF TIME
IN RESPONSE TO OFFICE ACTION

The Honorable Commissioner of Patents
UNITED STATES PATENT OFFICE
220 20th Street S.
Crystal Plaza Two, Lobby, Room 1B03
Arlington, Virginia 22202

Dear Sir:

It is respectfully requested that the time for filing a response to the Office Action of February 17, 2004, now set to expire May 17, 2004, be extended for three months, to and including **August 17, 2004**.

Applicant encloses a cheque in the amount of **$950.00 US** for payment of the three-month extension of time fee for a large entity. If there is any deficiency or surplusage of the fees enclosed, please obtain any such deficiency from or credit the surplusage to Deposit Account No. 08-3255 and advise Applicant's Agent.

Respectfully submitted,

APOTEX INC.

July 28, 2004

By _____
Neil H. Hughes, P.Eng.
Registration No. 33,636
Agent for Applicant
175 Commerce Valley Drive West
Suite 200
Thornhill, ON L3T 7P6

08/02/2004 SSITHIB1 00000098 10311814
01 FC:1253 950.00 OP

PATENT APPLICATION FEE DETERMINATION RECORD
Effective October 1, 2001

Application or Docket Number: PC-153433 10/311,874

CLAIMS AS FILED - PART I

	(Column 1)	(Column 2)
TOTAL CLAIMS		
FOR	NUMBER FILED	NUMBER EXTRA
TOTAL CHARGEABLE CLAIMS	47 minus 20=	* 27
INDEPENDENT CLAIMS	14 minus 3 =	* 11
MULTIPLE DEPENDENT CLAIM PRESENT		☐

* If the difference in column 1 is less than zero, enter "0" in column 2

SMALL ENTITY TYPE ☐		OR	OTHER THAN SMALL ENTITY	
RATE	FEE		RATE	FEE
BASIC FEE		OR	BASIC FEE	890
X$ 9=		OR	X$18=	486
X42=		OR	X84=	924
+140=		OR	+280=	
TOTAL		OR	TOTAL	2300

CLAIMS AS AMENDED - PART II

AMENDMENT A

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	* 33	Minus	** 47	-
Independent	* 14	Minus	*** 14	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

SMALL ENTITY		OR	OTHER THAN SMALL ENTITY	
RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X42=		OR	X84=	
+140=		OR	+280=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X42=		OR	X84=	
+140=		OR	+280=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

AMENDMENT C

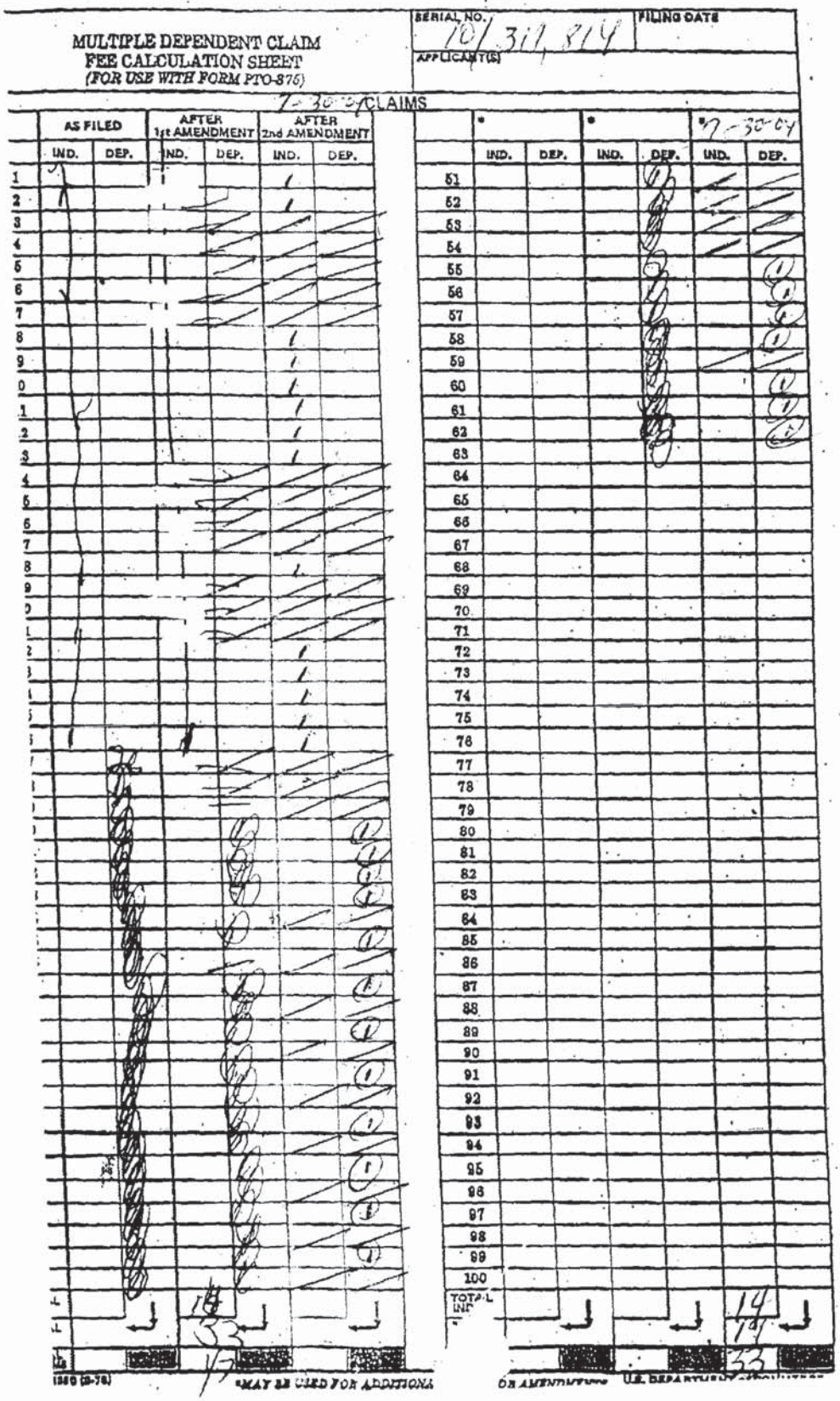
	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X42=		OR	X84=	
+140=		OR	+280=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20."
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3."
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

FORM PTO-875 (Rev. 8/01) — Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE

BEST AVAILABLE COPY



MULTIPLE DEPENDENT CLAIM
FEE CALCULATION SHEET
(FOR USE WITH FORM PTO-875)

SERIAL NO. 10/312,814
FILING DATE
APPLICANT(S)

7-30-04 CLAIMS

	AS FILED		AFTER 1st AMENDMENT		AFTER 2nd AMENDMENT		*		*		*7-30-04	
	IND.	DEP.	IND.	DEP.	IND.	DEP.	IND.	DEP.	IND.	DEP.	IND.	DEP.
1	1				1		51					
2	1				1		52					
3							53					
4							54					
5							55					1
6							56					1
7							57					1
8					1		58					1
9					1		59					
10					1		60					1
11					1		61					1
12					1		62					1
13					1		63					
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45							95					
46							96					
47							97					
48							98					
49							99					
50							100					
TOTAL IND							TOTAL IND					
TOTAL												

1980 (8-78) *MAY BE USED FOR ADDITIONAL ... OR AMENDMENTS ... U.S. DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/311,814	04/04/2003	Michael Spino	PC-1834033	2281

23607 7590 08/13/2004

IVOR M. HUGHES, BARRISTER & SOLICITOR,
PATENT & TRADEMARK AGENTS
175 COMMERCE VALLEY DRIVE WEST
SUITE 200
THORNHILL, ON L3T 7P6
CANADA

EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 08/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450
www.uspto.gov

Paper No.

Notice of Non-Compliant Amendment (37 CFR 1.121)

The amendment document filed on 7-30-04 is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121, as amended on June 30, 2003 (see *68 Fed. Reg. 38611*, Jun. 30, 2003). In order for the amendment document to be compliant, correction of the following item(s) is required. **Only the corrected section of the non-compliant amendment document must be resubmitted (in its entirety), e.g., the entire "Amendments to the claims" section of applicant's amendment document must be re-submitted.** 37 CFR 1.121(h).

THE FOLLOWING CHECKED (X) ITEM(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

☐ 1. Amendments to the specification:
- ☐ A. Amended paragraph(s) do not include markings.
- ☐ B. New paragraph(s) should not be underlined.
- ☐ C. Other_____

☐ 2. Abstract:
- ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
- ☐ B. Other_____

☐ 3. Amendments to the drawings: _____

☒ 4. Amendments to the claims:
- ☒ A. A complete listing of all of the claims is not present.
- ☐ B. The listing of claims does not include the text of all claims (including withdrawn claims)
- ☐ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified.
- ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
- ☐ E. Other: _____

For further explanation of the amendment format required by 37 CFR 1.121, see MPEP Sec. 714 and the USPTO website at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/officeflyer.pdf .

If the non-compliant amendment is a **PRELIMINARY AMENDMENT,** applicant is given ONE MONTH from the mail date of this letter to supply the corrected section which complies with 37 CFR 1.121. Failure to comply with 37 CFR 1.121 will result in non-entry of the preliminary amendment and examination on the merits will commence without consideration of the proposed changes in the preliminary amendment(s). This notice is not an action under 35 U.S.C. 132, and **this ONE MONTH time limit is not extendable.**

If the non-compliant amendment is a reply to a **NON-FINAL OFFICE ACTION (including a submission for an RCE),** and since the amendment appears to be a *bona fide* attempt to be a reply (37 CFR 1.135(c)), applicant is given a TIME PERIOD of ONE MONTH from the mailing of this notice within which to re-submit the corrected section which complies with 37 CFR 1.121 in order to avoid abandonment. **EXTENSIONS OF THIS TIME PERIOD ARE AVAILABLE UNDER 37 CFR 1.136(a).**

If the amendment is a reply to a **FINAL REJECTION,** this form may be an attachment to an Advisory Action. **The period for response to a final rejection continues to run from the date set in the final rejection**, and is not affected by the non-compliant status of the amendment.

Cecelia Belancourt — 571-272-0509

Legal Instruments Examiner (LIE) — Telephone No.

Rev. 10/03

IN THE UNITEDSTATES PATENT OFFICE

Patent Application Serial No.: 10/311,814

Our Ref: PC-1834033
CUSTOMER NO. 23607

Applicants: Apotex Inc.

Agent: Neil H. Hughes, P. Eng.
c/o Ivor M. Hughes
Barrister & Solicitor
Patent & Trade Mark Agents
Suite 200,
175 Commerce Valley Dr. W.
Thornhill, Ontario.
L3T 7P6, CANADA

Title: A NEW USE FOR DEFERIPRONE

Inventors: Michael Spino and Antonio Piga

Examiner: Raymond J. Henley III

Group Art Unit: 1614 **Due Date: September 13, 2004**

No. of Pages including this sheet: 10

DELIVERED TO FACSIMILE NO. (703) 872-9306

August 23, 2004

Commissioner of Patents
U.S. Patent and Trademark Office
220 20th Street S.
Crystal Plaza Two, Lobby, Room 1B03
Arlington, VA 22202

Attention: Ms. Coralia Betancourt
Legal Instruments Examiner (LIE)

Dear Ms. Betancourt:

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper:
1) Letter to Commissioner of Patents dated August 23, 2004
2) Copy of Notice of Non-Compliant Amendment dated August 13, 2004
3) A complete listing of all claims included in Response filed on July 30, 2004

is being facsimile transmitted to the United States Patent Office Facsimile No. (703) 872-9306 on the date shown below.

NEIL H. HUGHES
Agent for Applicant

Signature: Date: August 23, 2004

Ivor M. Hughes
Barrister & Solicitor
Patent & Trade Mark Agents
Canada, United States

Barristers & Solicitors
Ivor M. Hughes
Rick Tuzi
Mark Ng
Patent Agents
Neil H. Hughes, P.Eng.
Marcelo K. Sarkis, P.Eng.
Wm. Kitz Sinden

OFFICIAL

Our Ref.: PC-1834033

August 23, 2004

VIA FACSIMILE 703-872-9306

The Commissioner of Patents
UNITED STATES PATENT OFFICE
220 20th Street S.
Crystal Plaza Two, Lobby, Room 1B03
Arlington, Virginia 22202

Attention: Ms. Coralia Betancourt
Legal Instruments Examiner (LIE)

Dear Ms. Betancourt:

Re: United States Patent Application Serial No. 10/311,814
of Apotex Inc.
for A NEW USE FOR DEFERIPONE
Inventors: Michael Spino and Antonio Piga
Examiner: Raymond J. Henley III
Customer No. 23607
Due Date: September 13, 2004

Further to the Notice of Non-Compliant Amendment (37 CFR 1.121) dated August 13, 2004, a copy of which is enclosed herewith, Applicant encloses a complete listing of all claims included in the Response to Official Action of February 17, 2004 filed with the United States Patent Office on July 30, 2004.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Registration No. 33,636
Agent for Applicant

NHH/lvp
Enclosure

175 Commerce Valley Dr. W., Suite 200, Thornhill, Ontario, Canada L3T 7P6 Phone: 905 771-6414 Fax: 905 771-6420
website: www.ivormhughes.com email: mail@ivormhughes.com

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/311,814	04/04/2003	Michael Spino	PC-1834033	2281

23607 7590 08/13/2004

IVOR M. HUGHES, BARRISTER & SOLICITOR,
PATENT & TRADEMARK AGENTS
175 COMMERCE VALLEY DRIVE WEST
SUITE 200
THORNHILL, ON L3T 7P6
CANADA

EXAMINER	
HENLEY III, RAYMOND J	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 08/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450
www.uspto.gov

Paper No.

Notice of Non-Compliant Amendment (37 CFR 1.121)

The amendment document filed on 7-30-04 is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121, as amended on June 30, 2003 (*see 68 Fed. Reg. 38611*, Jun. 30, 2003). In order for the amendment document to be compliant, correction of the following item(s) is required. **Only the corrected section of the non-compliant amendment document must be resubmitted (in its entirety), e.g., the entire "Amendments to the claims" section of applicant's amendment document must be re-submitted.** 37 CFR 1.121(h).

THE FOLLOWING CHECKED (X) ITEM(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

☐ 1. Amendments to the specification:
- ☐ A. Amended paragraph(s) do not include markings.
- ☐ B. New paragraph(s) should not be underlined.
- ☐ C. Other _____

☐ 2. Abstract:
- ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
- ☐ B. Other _____

☐ 3. Amendments to the drawings: _____

☒ 4. Amendments to the claims:
- ☒ A. A complete listing of all of the claims is not present.
- ☐ B. The listing of claims does not include the text of all claims (including withdrawn claims)
- ☐ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified.
- ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
- ☐ E. Other: _____

For further explanation of the amendment format required by 37 CFR 1.121, see MPEP Sec. 714 and the USPTO website at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/officeflyer.pdf.

If the non-compliant amendment is a **PRELIMINARY AMENDMENT**, applicant is given ONE MONTH from the mail date of this letter to supply the corrected section which complies with 37 CFR 1.121. Failure to comply with 37 CFR 1.121 will result in non-entry of the preliminary amendment and examination on the merits will commence without consideration of the proposed changes in the preliminary amendment(s). This notice is not an action under 35 U.S.C. 132, and **this ONE MONTH time limit is not extendable.**

If the non-compliant amendment is a reply to a **NON-FINAL OFFICE ACTION (including a submission for an RCE)**, and since the amendment appears to be a *bona fide* attempt to be a reply (37 CFR 1.135(c)), applicant is given a TIME PERIOD of ONE MONTH from the mailing of this notice within which to re-submit the corrected section which complies with 37 CFR 1.121 in order to avoid abandonment. **EXTENSIONS OF THIS TIME PERIOD ARE AVAILABLE UNDER 37 CFR 1.136(a).**

If the amendment is a reply to a **FINAL REJECTION**, this form may be an attachment to an Advisory Action. **The period for response to a final rejection continues to run from the date set in the final rejection**, and is not affected by the non-compliant status of the amendment.

Coralie Betancourt — Legal Instruments Examiner (LIE)

571-272-0509 — Telephone No.

Rev. 10/03

IN THE CLAIMS

1. (currently amended) A method of treating iron induced cardiac disease in a **heavily transfused** patient **experiencing an** ~~with~~ iron overload **condition of the heart**, ~~such as in thalassemia or the like~~ **said method** comprising administering to the **heavily transfused** patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to **stabilize/reduce/iron accumulation in the heart resulting from being heavily transfused and preventing further iron accumulation in the heart normally associated with** ~~treat~~ iron induced cardiac disease ~~normally associated with iron overload~~.

2. (currently amended) A method of preventing iron induced cardiac disease in a **heavily transfused** patient **experiencing an** ~~with~~ iron overload **condition of the heart**, ~~such as in thalassemia or the like~~ **said method** comprising administering to the **heavily transfused** patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to **prevent further iron accumulation in the heart normally associated with** ~~treat~~ iron induced cardiac disease ~~normally associated with iron overload~~.

3-7 (cancelled)

8. (currently amended) ~~An~~ **A pharmaceutical composition for iron induced cardiac disease comprising an** effective therapeutic amount of **the orally administered iron chelator** deferiprone or a physiologically acceptable salt thereof for the prevention of ~~the risk of~~ heart disease in **heavily transfused** patients ~~having~~ **risking an** iron overload **condition of the heart**, ~~such as in thalassemia or the like, comprising an effective amount of deferiprone or a physiologically acceptable salt thereof~~ **said therapeutic amount being** sufficient to ~~treat~~ **prevent further iron accumulation in the heart associated with** iron induced cardiac disease ~~normally associated with iron overload~~.

9. (currently amended) ~~An~~ **A pharmaceutical composition for iron induced cardiac disease comprising an** effective therapeutic amount of **the orally administered iron chelator** deferiprone or a physiologically acceptable salt thereof for the stabilization of ~~the risk of~~ heart disease in **heavily transfused** patients ~~having~~ **experiencing** iron overload **of the heart**, ~~such as in thalassemia or the like comprising an effective amount of deferiprone or a physiologically acceptable salt thereof~~ **said therapeutic amount being** sufficient to **stabilize iron accumulation in the heart and prevent further iron accumulation in the heart associated with** ~~treat~~ iron induced cardiac disease ~~normally associated with iron overload~~.

10. (currently amended) ~~An~~ **A pharmaceutical composition for iron induced cardiac disease comprising an** effective therapeutic amount of **the orally administered iron chelator** deferiprone or a physiologically acceptable salt thereof for the reduction ~~of the risk~~ **in the level of iron burden in the heart** ~~of heart disease~~ in **heavily transfused** patients ~~having~~ **experiencing** iron overload **of the heart**, ~~such as in thalassemia or the like comprising an effective amount of deferiprone or a physiologically acceptable salt thereof~~ **said therapeutic amount being** sufficient to ~~treat~~ **reduce** iron **burden in the heart and the resulting iron** induced cardiac disease ~~normally associated with iron overload~~.

11. (currently amended) A method of preventing ~~the risk of~~ heart disease in **heavily transfused** patients ~~having~~ **risking** iron overload **of the heart**, ~~such as in thalassemia or the like~~ comprising the administration of a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to ~~treat~~ **prevent** iron induced cardiac disease ~~normally associated with iron overload~~.

12. (currently amended) A method of stabilizing ~~the risk of~~ heart disease in **heavily transfused** patients having iron overload, ~~such as in thalassemia or the like~~ comprising the administration of a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to treat iron **burden in the heart normally associated with** induced cardiac disease ~~normally associated with iron overload~~.

13. (currently amended) A method of reducing ~~the risk of~~ **the iron burden in the heart associated with** heart disease in **heavily transfused** patients having iron overload, ~~such as in thalassemia or the like~~ comprising the administration of a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to ~~treat~~ **reduce the iron burden of the heart normally associated with** iron induced cardiac disease ~~normally associated with iron overload~~.

14-17 (cancelled)

18. (currently amended) A **pharmaceutical composition for iron induced cardiac disease comprising a** therapeutically effective amount of **the iron chelator** deferiprone or physiologically acceptable salt thereof for the prevention, treatment, or reversal of heart disease in **heavily transfused** patients ~~having~~ **risking or experiencing** an iron overload condition of the heart, ~~comprising an effective amount of deferiprone or a physiologically acceptable salt thereof~~ **said therapeutic amount being sufficient** to ~~preferentially~~ reduce the iron stores in the heart **and** in ~~comparison~~ **preference** to the iron stores in less critical organs/tissue in the body.

19-21 (cancelled)

22. (currently amended) A method of treating~~/preventing/or reversing~~ heart disease in a **heavily transfused** patient having an iron overload condition of the heart comprising administering to the patient a therapeutically effective amount of deferiprone, or a physiologically acceptable salt thereof in order to ~~preferentially~~ reduce the iron stores in the heart in ~~comparison~~ **preference** to less critical organs/tissue in the body.

23. (currently amended) A method of ~~treating/~~preventing~~/or reversing~~ heart disease in **heavily transfused** patients having an iron overload condition of the heart comprising administering to the patient a therapeutically ~~effective~~ amount of ~~deferiprone~~ or a physiologically acceptable salt thereof to ~~preferentially reduce~~ **chelate** the iron stores in the heart in ~~comparison~~ **preference** to the iron stores in less critical organs/tissue in the body.

24. (currently amended) A method of ~~treating/preventing/or~~ reversing heart disease in **heavily transfused** patients having an iron overload condition of the heart comprising administering to the patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof to ~~preferentially~~ reduce the iron stores in the heart in ~~comparison~~ **preference** to the iron stores in less critical organs/tissue in the body.

25. (currently amended) A method of treatment, prevention, or reversal of heart disease in a **heavily transfused** patient having an iron overload condition of the heart comprising administering to the patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof for the direct ~~preferential~~ reduction/removal of ~~iron (for example~~ intracellular iron~~)~~ stores in the heart.

26. (currently amended) A method to prevent/treat/reverse the occurrence of iron-induced cardiac disease in **heavily transfused** patients with an iron overload condition ~~such as thalassemia or the like~~, comprising administering to said patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof, wherein deferiprone's efficacy is cardio preferential when compared with its ability to lower total iron stores in the body.

27-29 (cancelled)

30. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising the~~ **wherein** ~~active ingredient~~ deferiprone or a physiologically acceptable salt thereof **is administered orally** for preventing the risk of heart disease in patients having iron overload.

31. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising the~~ **wherein** ~~active ingredient~~ deferiprone or a physiologically acceptable salt thereof **is administered orally** for stabilizing the risk of heart disease in patients having iron overload.

32. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising the~~ **wherein** ~~active ingredient~~ deferiprone or a physiologically acceptable salt thereof **is administered orally** for reducing the risk of heart disease in patients having iron overload.

33. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising an oral dosage form of~~ **wherein** deferiprone or a physiologically acceptable salt thereof **is present is an oral dosage form** with other excipients.

34. (cancelled)

35. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising daily~~ **wherein the** administration **frequency to the patient** of an amount of deferiprone or a physiologically acceptable salt thereof **is daily and** substantially in the range of up to 150mg~~/kg to the patient.~~ **per kilogram of body weight.**

36. (cancelled)

37. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising~~ **wherein the** administration **frequency to the patient** of a ~~daily~~ dosage amount of deferiprone or a physiologically acceptable salt thereof **is daily and** substantially in the range of up to 125 mg~~/kg to the patient.~~ **per kilogram of body weight.**

38. (cancelled)

39. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 ~~further comprising~~ **wherein the** administration **frequency to the patient** of a ~~daily~~ dosage amount of deferiprone or a physiologically acceptable salt thereof **is daily and** substantially in the range of 25mg~~/kg~~ to 75mg~~/kg to the patient.~~ **per kilogram of body weight.**

40. (cancelled)

41. (original) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 wherein deferiprone is administered in a manner selected from the group of intravenously, transdermally, rectally, orally, bucally, or aurally.

42. (cancelled)

43. (original) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 wherein deferiprone is administered orally.

44. (cancelled)

45. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 wherein ~~the dosage form~~ **deferiprone or a physiologically acceptable salt thereof** is **in** a sustained release formulation.

46. (cancelled)

47. (original) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 wherein deferiprone has a cardio preferred/selective function when compared to desferrioxamine or other alternative chelating agents utilized in patients suffering iron overload.

48. (cancelled)

49. (original) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 and 26 wherein deferiprone is administered in addition to desferrioxamine.

50. (cancelled)

51. (cancelled)

52. (cancelled)

53. (cancelled)

54. (cancelled)

55. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 ~~further comprising~~ **wherein said composition is administered to the patient** daily ~~administration of an amount of deferiprone or a physiologically acceptable salt thereof~~ **and** substantially in the range of up to 150mg~~/kg to the patient.~~ **per kilogram of body weight.**

56. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 ~~further comprising administration of a~~ **wherein said composition is administered to the patient** daily ~~dosage amount of deferiprone or a physiologically acceptable salt thereof~~ **and** substantially in the range of up to 125 mg~~/kg to the patient.~~ **per kilogram of body weight.**

57. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 ~~further comprising administration of a~~ **wherein said composition is administered to the patient** daily ~~dosage amount of deferiprone or a physiologically acceptable salt thereof~~ **and** substantially in the range of 25mg~~/kg~~ to 75mg~~/kg to the patient.~~ **per kilogram of body weight.**

58. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 wherein ~~deferiprone~~ **the composition** is administered in a manner selected from the group of intravenously, transdermally, rectally, orally, bucally, or aurally.

59. (cancelled)

60. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 wherein the ~~dosage form~~ **composition** is **in** a sustained release formulation.

61. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 wherein ~~deferiprone~~ **said composition** has a cardio preferred/selective function when compared to desferrioxamine or other alternative chelating agents utilized in patients suffering iron overload.

62. (currently amended) The ~~effective therapeutic amount~~ **composition** of claims 8, 9, 10 and 18 wherein ~~deferiprone~~ **the composition** is administered in addition to desferrioxamine.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/311,814	04/04/2003	Michael Spino	PC-1834033	2281

23607 7590 09/08/2004

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EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	10/311,814	SPINO ET AL.	
	Examiner	Art Unit	
	Raymond J Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2004 and 23 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,8-13,18,22-26,30-33,35,37,39,41,43,45,47,49,55-58 and 60-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,8-13,18,22-26,30-33,35,37,39,41,43,45,47,49,55-58 and 60-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 1, 2, 8-13, 18, 22-26, 30-33, 35, 37, 39, 41, 43, 45, 47, 49, 55-58 AND 60-62 ARE PRESENTED FOR EXAMINATION

Applicants' Amendments filed July 30, 2004 and August 23, 2004 have been received and entered into the application.

Accordingly, the specification at page 1 and claims 1, 2, 8-13, 18, 22-26, 30-33, 35, 37, 39, 45, 55-58 and 60-62 have been amended; the abstract has been added; and claims 51-54 and 59 have been canceled.

In light of Applicants' amendments and comments at pages 9-20 of their amendment filed August 23, 2004, the only remain issues are those presented herein. The objections/rejections set forth in the previous Office action not set forth herein are withdrawn.

Claim Objection

Claims 30-33, 35, 37, 39, 41, 43, 45, 47, 49, 55-58 and 60-62 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must refer to other claims in the alternative only. See MPEP § 608.01(n). In order to overcome this objection, application should change in the above claims the "and" in the listing of the dependent claims to ---or---.

Claims 55-58 and 62 are also objected to as not being further limiting. These claims depend from claims directed to compositions and yet set forth method limitations, i.e., "is administered". Method limitations do not further limit compositions of matter. Also, in claims 55-57 the unit of measurement "mg per kilogram of body weight" is improper because measurements of ingredients contained in the composition should relate to the composition, i.e.,

per unit volume or weight of the composition, and not to a feature, i.e., a patient, that is not apart of the composition, i.e., outside the scope of the claim, and which is variable, i.e., dependent on the weight of the patient.

Claim Rejection - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-13, 22-25, 30-33, 35, 37, 39, 41, 43, 45, 47 and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment, prevention, stabilization or reversal of iron induced cardiac/heart disease, does not reasonably provide enablement for the treatment, prevention, stabilization or reversal of cardiac/heart disease in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The present specification is evaluated by the Examiner as directed by the Court in *In re Marzocchi et al.* , 169 USPQ 367 (CCPA 1971):

"Specification disclosure which contains teaching of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with enabling requirement of first paragraph of 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contain therein which must be relied on for enabling support*; assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in specification is truly enabling." (emphasis added).

Here, the objective truth of the statement that a cardiac/heart disease in general could be treated, prevented, stabilized or reversed is doubted because the there is not known in the

medical/pharmaceutical art, any one particular therapeutic agent or combination of therapeutic agents that is/are capable of treating, preventing, stabilizing or reversing all known cardiac/heart diseases. Also, applicants' specification is directed solely to iron-induced cardiac/heart diseases.

Accordingly, the claims are deemed properly rejected.

Claim Rejection - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 8-13, 18, 22-26, 30-33, 35, 37, 39, 41, 43, 45, 47, 49, 55-58 and 60-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "heavily transfused" in the claims is a relative term that renders the claim indefinite. The term "heavily" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejection - 35 USC § 102

Claims 8, 9, 10, 18, 55-58 and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by any one of Olivieri et al., Hoffbrand et al. (Examiner cit. Ref. "U") or Hoffbrand et al. (Examiner cit. Ref. "V"), each of record, for the reasons of record as set forth in the previous Office action as applied to claims 8, 9, 10, 18 and 51-59.

Claim Rejection - 35 USC § 103

Claims 8, 9, 10, 18, 55-58 and 60-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olivieri et al., Hoffbrand et al. (Examiner cit. Ref. "U") or Hoffbrand et al. (Examiner cit. Ref. "V"), as above in view of Lai (U.S. Patent No. 5,922,761), each of record.

The differences between the above and the claimed subject matter lies in that the references fail to teach the presently claimed dosage forms or the addition of desferrioxamine.

However, to the skilled artisan, the claimed subject matter would have been obvious because various dosage forms were known to the skilled artisan and the selection of any given dosage form would have been a matter well within the purview of the skilled artisan, based upon the preference or need of the particular patient being treated. Also, the additional use of desferrioxamine would have been obvious because Lai teaches desferrioxamine (see previous Office action at page 6) for the same purpose and it has been held that it is considered prima facie obvious to have combined two or more ingredients each of which was known to be useful for the same purpose in order to form a third composition that is useful for the very same purpose. The idea for combining them flows logically from their have been used separately. See In re Kerkhoven 205 U.S.P.Q. 1069 (CCPA 1980) and the cases cited therein. The skilled artisan would have been motivated to combine such ingredients in order to achieve at least additive results and to provide the individual being treated with the most convenient, effective therapy possible.

Applicants' Arguments

Applicants' arguments at pages 9-20 of their amendment filed August 23, 2004 have been carefully considered, but fail to persuade the Examiner of error in his determinations above.

In particular, applicants' comments and arguments are based upon the novel or unobvious **use** of deferiprone. These arguments, however, are not commensurate in scope with the claimed subject matter presently rejected that is directed to compositions of matter. Applicants' attention is drawn to In re Dillon, 16 USPQ2nd, 1897 at 1900 (CAFC 1990). The court sitting in banc ruled that the recitation of a new utility for an old and well known or otherwise obvious composition does not render that composition new or nonobvious.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

September 2, 2004

Index of Claims

Application No.	Applicant(s)
10/311,814	SPINO ET AL.
Examiner	**Art Unit**
Raymond J. Henley III	1614

√	Rejected	–	(Through numeral) Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

Claim Final	Claim Original	Date 2/3/04	Date 9/2/04
	1	✓	✓
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Claim Final	Claim Original	Date 2/3/04	Date 9/2/04
	51	✓	
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U.S. Patent and Trademark Office

Part of Paper No. 02032004

Search Notes

Application No.	Applicant(s)	
10/311,814	SPINO ET AL.	
Examiner	**Art Unit**	
Raymond J. Henley III	1614	

SEARCHED

Class	Subclass	Date	Examiner
514	348	2/2/2004	RJH
↓	616	↓	↓
updated		9/2/04	TH

INTERFERENCE SEARCHED

Class	Subclass	Date	Examiner

SEARCH NOTES (INCLUDING SEARCH STRATEGY)

	DATE	EXMR
STN Search: CAPLUS, USPATFULL, MEDLINE	2/2/2004	RJH
Palm Inventor Name Search: - Michael Spino - Antonio Piga	↓	↓
updated	9/2/04	TH

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Our Ref.: PC-1834033

December 7, 2004

VIA COURIER

U.S. Patent and Trademark Office
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Arlington, Virginia 22202 U.S.A.

Dear Sir:

Re: Response to Examination Report
Application Serial No. 10/311,814 filed on April 4, 2003
of Michael Spino and Antonio Spiga
for A NEW USE FOR DEFERIPRONE
Group Art Unit: 1614
Examiner: Raymond J. Henley III
Due Date: DECEMBER 8, 2004
CUSTOMER NO. 23607

Please find enclosed herewith the following:

1. Response to Examination Report dated December 6, 2004;
2. Fee Transmittal For FY 2005;
3. Transmittal Form;
4. Information Disclosure Statement;
5. CD with references cited in the Information Disclosure Statement;
6. Cheque in the amount of $180.00.

If there should occur an overpayment or an underpayment of fees in respect of this submission, the Commissioner is authorized to access Deposit Account Number 08-3255 to make the appropriate adjustments and advise Applicant's agent;

Also enclosed herewith is a stamped, self-addressed verification card which we request that you kindly acknowledge and return to this office at the earliest opportunity. We thank the Commissioner for his cooperation in this regard and look forward to receiving filing data in this matter.

175 Commerce Valley Dr. W., Suite 200, Thornhill, Ontario, Canada L3T 7P6 Phone: 905 771-6414 Fax: 905 771-6420
website: www.ivormhughes.com email: mail@ivormhughes.com

We thank the Patent Office for its cooperation in this regard and look forward to receiving filing data in this matter.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Agent for Applicant
Registration No. 33,636

NHH:md
Enclosures

PTO/SB/21 (09-04)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

Application Number	10/311,814
Filing Date	April 4, 2003
First Named Inventor	Michael Spino
Art Unit	1614
Examiner Name	Raymond J. Henley II
Attorney Docket Number	PC-1834033

ENCLOSURES *(Check all that apply)*

- [x] Fee Transmittal Form
- [x] Fee Attached
- [ ] Amendment/Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [x] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
  - [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
  - [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- [ ] Proprietary Information
- [ ] Status Letter
- [ ] Other Enclosure(s) (please Identify below):

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Ivor M. Hughes		
Signature			
Printed name	Neil H. Hughes		
Date	Dec. 6/04	Reg. No.	33,636

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature			
Typed or printed name		Date	

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PTO/SB/17 (11-04)
Approved for use through 07/31/2006 OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Effective on 10/01/2004. Patent fees are subject to annual revision.

FEE TRANSMITTAL
For FY 2005

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($)180.00

Complete if Known	
Application Number	10/311,814
Filing Date	April 4, 2003
First Named Inventor	Michael Spino
Examiner Name	Raymond J. Henley III
Art Unit	1614
Attorney Docket No.	PC-1834033

METHOD OF PAYMENT (check all that apply)

☒ Check ☐ Credit Card ☐ Money Order

☒ Deposit Account ☐ None

Deposit Account Number: 08-3255

Deposit Account Name: Ivor M. Hughes

The Director is hereby authorized to: (check all that apply)

☐ Charge fee(s) indicated below

☐ Charge fee(s) indicated below, except for the filing fee

☒ Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17

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FEE CALCULATION

1. BASIC FILING FEE

Fee Description	Fee ($)	Small Entity Fee ($)	Fee Paid($)
Utility Filing Fee	790	395	
Design Filing Fee	350	175	
Plant Filing Fee	550	275	
Reissue Filing Fee	790	395	
Provisional Filing Fee	160	80	

Subtotal (1) $ _____

FEE CALCULATION (continued)

2. EXTRA CLAIM FEES

Fee Description	Fee ($)	Small Entity Fee ($)
Each claim over 20	18	9
Each independent claim over 3	88	44
Multiple dependent claims	300	150
For Reissues, each claim over 20 and more than in the original patent	18	9
For Reissues, each independent claim more than in the original patent	88	44

Total Claims	Extra Claims	Fee ($)	Fee Paid ($)
_____ - 20 or HP =	_____	x _____	= _____

HP = highest number of total claims paid for, if greater than 20

Indep. Claims	Extra Claims	Fee ($)	Fee Paid ($)
_____ - 3 or HP =	_____	x _____	= _____

HP = highest number of independent claims paid for, if greater than 3

Multiple Dependent Claims	Fee ($)	Fee Paid ($)
	_____	_____

Subtotal (2) $ _____

3. OTHER FEES

Fee Description	Fee ($)	Small Entity Fee ($)	Fee Paid($)
1-month extension of time	110	55	
2-month extension of time	430	215	
3-month extension of time	980	490	
4-month extension of time	1,530	765	
5-month extension of time	2,080	1,040	
Information disclosure stmt. fee	180	180	180.00
37 CFR 1.17(q) processing fee	50	50	
Non-English specification	130	130	
Notice of Appeal	340	170	
Filing a brief in support of appeal	340	170	
Request for oral hearing	300	150	
Other: _____			

Subtotal (3) $ 180.00

SUBMITTED BY

Signature		Registration No. (Attorney/Agent) 33,636	Telephone 905-771-6414
Name (Print/Type)	Neil H. Hughes		Date Dec. 6/04

IN THE UNITED STATES PATENT OFFICE

CUSTOMER NO. 23607

Application Serial No. 10/311,814 Our Ref.: PT-1834033

Applicant: Apotex Inc.

Neil H. Hughes, P.Eng.
Ivor M. Hughes,
Barrister & Solicitor
Patent & Trademark Agents
Suite 200,
175 Commerce Valley Dr. W.
Thornhill, Ontario
Canada L3T 7P6

Title: A NEW USE FOR DEFERIPRONE

Inventors: Michael Spino and Antonio Piga

Group Art Unit: 1614

INFORMATION DISCLOSURE STATEMENT

December 6, 2004

VIA COURIER

U.S. Patent and Trademark Office
220 20th Street South
Customer Window, Mail Stop Amendment
Crystal Plaza Two, Lobby Room 1B03
Arlington, VA, 22202

Dear Sir:

Applicants and the undersigned are aware of "patents, publications, or other information" which they believe may be material to the examination of the above-identified application. Applicants have attached Form 1449 (14 pages) along with a CD with the prior art as references in Form 1449 pursuant to 37 C.F.R. §§ 1.97-1.99

and to the duty of disclosure set forth in 37. C.F.R. § 1.56. Applicant also encloses herewith the required fee of $180.00. If there is any deficiency or surplusage of the fees required for this application, please obtain any such deficiency or credit the surplusage to Deposit Account 08-3255 and advise Applicants' Agent.

Although this Information Disclosure Statement identifies references which may be "material," it is not intended to constitute an admission that any patent, publication, or other information referred to is "prior art" (within the meaning of 35 U.S.C. §102 and §103) as to the invention disclosed and claimed in this application unless specifically designated as such. Moreover, no representation is intended as to the relative relevance of any portion of the references or as to the relevance among references, whether cited in this Statement or elsewhere.

In accordance with 37 C.F.R. §1.97(b), the filing of this Information Disclosure Statement shall not be construed to mean that a novelty search has been made or that no other information which may be material (as defined in 37 C.F.R. §1.56(a)) exists.

1. Gabutti V, Piga A. Results of Long-Term Iron-Chelating Therapy. Acta Haematol 1996; 95:26-36.

2. Wolfe LC, Olivieri NF, Sallan D, Colan S, Rose V, Propper RD et al. Prevention of cardiac disease by subcutaneous desferrioxamine in patients with thalassemia major. N Engl J Med 1985; 312(25): 1600-1603.

3. Aldouri MA, Wonke B. Hoffbrand AV, Flynn DM, Ward SE, Agnew JE et al. High Incidence of Cardiomyopathy in Beta-Thalassemia Patients Receiving Regular Transfusion and Iron Chelation: Reversal by Intensified Chelation. Acta Haematol 1990; 84:113-117.

4. Brittenham GM, Griffith PM, Nienhuis AW, McLaren CE, Young NS, Tucker EE et al. Efficacy of Desferrioxamine in Preventing Complications of Iron Overload in Patients with Thalassemia Major. N Engl J Med 1994; 331(9):567-573.

5. Giardina PJV, Ehlers KH, Engle MA, Grady RW, Hilgartner MW. The Effect of Subcutaneous Desferrioxamine on the Cardiac Profile of Thalassemia Major: A Five-Year Study. Ann N Y Acad Sci 1985; 445:282-292.

6. Borgna-Pignatti C, Rugologgo S, DeStefano P, Piga A, et al. Survival and Disease Complications in Thalassemia Major. Ann N Y Acad Sci 1998; 850:227-231.

7. Olivieri NF, Nathan DG, MacMillan JH, Wayne AS, Liu P, McGee A et al. Survival in Medically Treated Patients with Homozygous Beta-Thalassemia. N Engl J Med 1994; 331(9):574-578.

8. Addis A, Loebstein R, Koren G, Einarson TR. Meta-analytic review of the clinical effectiveness of oral deferiprone (Deferiprone). Eur J Clin Pharmacol 1999; 55:1-6.

9. Grady RW, Hilgartner MW, Giardina PJV. Deferiprone: Its Effectiveness Relative to that of Desferrioxamine. 6th International Conference on Thalassemia and the Haemoglobinopathies, Abstract #2. 1997.

10. Olivieri NF, Brittenham GM, Armstrong SAM, Basran RK, Daneman R, Daneman N et al. First Prospective Randomized Trial of the Iron Chelators Deferiprone (Deferiprone) and Deferoxamine. Blood 86[10 Suppl. 1], 249a. 1995.

11. Olivieri NF, Belluzzo N, Muraca M, MacKenzie CC, Milone S, Polsinelli K et al. Evidence of Reduction in Hepatic, Cardiac and Pituitary Iron Stores in Patients with Thalassemia Major During Long-Term Therapy with the Orally Active Iron Chelating Agent Deferiprone. Blood 84[10 Suppl. 1], 109a. 1994.

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13. De Franceschi L, Shalev O, Piga A, Collell M, Olivieri O, Corrocher R et al. Deferiprone therapy in homozygous human beta-thalassemia removes erythrocyte membrane free iron and reduces KCI contransport activity. J Lab Clin Med 1999; 133:64-69.

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20. Hershko C, Graham G, Bates GW, Rachmilewitz EA. Non-Specific Serum Iron in Thalassemia: an Abnormal Serum Iron Fraction of Potential Toxicity. Br J Haematol 1978; 40: 255-263.

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51. Biochimica et biophysica acta molecular basis of disease. v1500 n3 (Mar 17, 2000) : p342-348. (Please note this reference is the same as *Biochimica et biophysica acta molecular basis of disease;* V.1500; No. 3; March 17/00; pp 342-348 - (Reference 59)).

52. Cohen AR, Martin MB. Iron chelation with oral deferiprone in patients with thalassemia. N Engl J Med. 1998 Dec 3;339(23):1713-4.

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Biochimica et biophysica acta molecular basis of disease: v1500 n3 (Mar 17, 2000): p342-348

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65. B. Wonke et al., Combined Therapy with Deferiprone and Desferrioxamine, British Journal of Haematology, 103, P361-183.

66. Orna Diav-Citrin et al., Oral Iron Chelation with Deferprone, New Frontiers in Pediatric Drug Therapy, 44(1) P235-247.

All of these references were cited in the background of the invention and are repeated for the purpose of fully discharging Applicant's duty of candor. These references were considered at the PCT phase as well. They are provided on a CD for convenience sake and to reduce the file size.

Full consideration of the materials presented is appreciated. These materials should have no impact on the merits of this case as submitted herewith.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Registration #33,636
Agent for Applicant

NHH:md
Enclosures

CITATION OF PRIOR ART

FORM PT0-1449 (REV. 8-83) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. **PC-1834033**	APPLICATION SERIAL NO. **10/311,814**
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)	APPLICANT **Apotex Inc.**	
CUSTOMER NO. 23607	FILING DATE **04/04/2003**	GROUP ART UNIT 1614

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		Gabutti V, Piga A. Results of Long-Term Iron-Chelating Therapy. Acta Haematol 1996; 95:26-36.
		Wolfe LC, Olivieri NF, Sallan D, Colan S, Rose V, Propper RD et al. Prevention of cardiac disease by subcutaneous desferrioxamine in patients with thalassemia major. N Engl J Med 1985; 312(25): 1600-1603.
		Aldouri MA, Wonke B. Hoffbrand AV, Flynn DM, Ward SE, Agnew JE et al. High Incidence of Cardiomyopathy in Beta-Thalassemia Patients Receiving Regular Transfusion and Iron Chelation: Reversal by Intensified Chelation. Acta Haematol 1990; 84:113-117.
		Brittenham GM, Griffith PM, Nienhuis AW, McLaren CE, Young NS, Tucker EE et al. Efficacy of Desferrioxamine in Preventing Complications of Iron Overload in Patients with Thalassemia Major. N Engl J Med 1994; 331(9):567-573.
		Giardina PJV, Ehlers KH, Engle MA, Grady RW, Hilgartner MW. The Effect of Subcutaneous Desferrioxamine on the Cardiac Profile of Thalassemia Major: A Five-Year Study. Ann N Y Acad Sci 1985; 445:282-292.
		Borgna-Pignatti C, Rugologgo S, DeStefano P, Piga A, et al. Survival and Disease Complications in Thalassemia Major. Ann N Y Acad Sci 1998; 850:227-231.

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

CITATION OF PRIOR ART

FORM PTO-1449 (REV. 8-83) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. PC-1834033	APPLICATION SERIAL NO. 10/311,814
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)	APPLICANT Apotex Inc.	
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FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO

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		Addis A, Loebstein R, Koren G, Einarson TR. Meta-analytic review of the clinical effectiveness of oral deferiprone (Deferiprone). Eur J Clin Pharmacol 1999; 55:1-6.
		Grady RW, Hilgartner MW, Giardina PJV. Deferiprone: Its Effectiveness Relative to that of Desferrioxamine. 6th International Conference on Thalassemia and the Haemoglobinopathies, Abstract #2. 1997.
		Olivieri NF, Brittenham GM, Armstrong SAM, Basran RK, Daneman R, Daneman N et al. First Prospective Randomized Trial of the Iron Chelators Deferiprone (Deferiprone) and Deferoxamine. Blood 86[10 Suppl. 1], 249a. 1995.

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		Olivieri NF, Belluzzo N, Muraca M, MacKenzie CC, Milone S, Polsinelli K et al. Evidence of Reduction in Hepatic, Cardiac and Pituitary Iron Stores in Patients with Thalassemia Major During Long-Term Therapy with the Orally Active Iron Chelating Agent Deferiprone. Blood 84[10 Suppl. 1], 109a. 1994.
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CITATION OF PRIOR ART

FORM PT0-1449 (REV. 8-83) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. PC-183408B	APPLICATION SERIAL NO. 10/311,814
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)	APPLICANT Apotex Inc.	
CUSTOMER NO. 23607	FILING DATE 04/04/2003	GROUP ART UNIT 1614

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		Hider RC, Kayyli R, Evans P, Mackinnon S. The production of Hydroxyl Radicals by Deferiprone-iron compounds under physiological conditions. Blood 94[10], 406a. 1999.
		Engle MA, Erlandson M, Smith CH. Late Cardiac Complications of Chronic, Severe, Refractory Anemia with Hemochromatosis. Circulation 1964; 30:698-705.
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		Sirchia G, Zanella A. A Short Guide to the Management of Thalassemia. Thalassemia Today: the Mediterranean Experience. 1987: 635-670.

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		Engle MA, Erlandson M, Smith CH. Late Cardiac Complications of Chronic, Severe, Refractory Anemia with Hemochromatosis. Circulation 1964; 30:698-705.
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		Berdoukas V, Bohans T. The Effect of Liver Iron on Cardiac Function. 10th International Conference on Oral Chelators in the treatment of Thalassemia and other diseases and Biomed Meeting 10, 13. 2000.
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		B. Wonke et al., Combined Therapy with Deferiprone and Desferrioxamine, British Journal of Haematology, 103, P361-183
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Doc Code: Artifact Artifact Type Code: Z

March 8, 2004

IN THE UNITED STATES PATENT OFFICE

Application Serial No. 10/311,814

Our Ref.: PC-1834033
CUSTOMER NO. 23607

Applicant: Apotex Inc.

Agent: Neil H. Hughes, P.Eng.
c/o Ivor M. Hughes
Barrister & Solicitor
Patent & Trade Mark Agents
Suite 200
175 Commerce Valley Dr. W.
Thornhill, Ontario
Canada L3T 7P6

Title: A NEW USE FOR DEFERIPRONE

Inventors: Michael Spino and Antonio Piga

Examiner: Raymond J. Henley III

Group Art Unit: 1614 **Due Date: December 8, 2004**

RESPONSE TO OFFICIAL ACTION
OF SEPTEMBER 8, 2004

December 6, 2004

VIA COURIER

U.S. Patent and Trademark Office
220 20th Street South
Customer Window, Mail Stop Amendment
Crystal Plaza Two, Lobby, Room 1B03
Arlington VA 22202

Dear Sir:

This submission is in response to the outstanding Official Action dated September 8, 2004 and due for response December 8, 2004. Should any fee be required for this submission or if there is any deficiency or surplusage of fees required please obtain any such fees or deficiency or credit the surplusage to Deposit Account 08-3255 and advise Applicants' Agent.

Please enter the following submissions:

IN THE CLAIMS

1. (currently amended) A method of treating iron induced cardiac disease in a ~~heavily transfused~~ transfusion dependent patient experiencing an iron overload condition of the heart, said method comprising administering to the ~~heavily transfused~~ patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to stabilize/reduce/iron accumulation in the heart resulting from being ~~heavily transfused~~ transfusion dependent and preventing further iron accumulation in the heart normally associated with iron induced cardiac disease.

2. (currently amended) A method of preventing iron induced cardiac disease in a ~~heavily transfused~~ transfusion dependent patient experiencing an iron overload condition of the heart, said method comprising administering to the ~~heavily transfused~~ transfusion dependent patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to prevent further iron accumulation in the heart normally associated with iron induced cardiac disease.

3-7 (cancelled)

8. (cancelled)

9. (cancelled)

10. (cancelled)

11. (currently amended) A method of preventing iron induced heart disease in ~~heavily transfused~~ transfusion dependent patients risking iron overload of the heart, comprising the administration of a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to prevent iron induced cardiac disease.

12. (currently amended) A method of stabilizing iron induced heart disease in ~~heavily transfused~~ transfusion dependent patients having iron overload, comprising the administration of a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to treat iron burden in the heart normally associated with iron induced cardiac disease.

13. (currently amended) A method of reducing the iron burden in the heart associated with iron induced heart disease in ~~heavily transfused~~ transfusion dependent patients having iron overload, comprising the administration of a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof sufficient to reduce the iron burden of the heart normally associated with iron induced cardiac disease.

14-17 (cancelled)

18. (cancelled)

19-21 (cancelled)

22. (currently amended) A method of treating iron induced heart disease in a ~~heavily transfused~~ transfusion dependent patient having an iron overload condition of the heart comprising administering to the patient a therapeutically effective amount of deferiprone, or a physiologically acceptable salt thereof in order to reduce the iron stores in the heart in preference to less critical organs/tissue in the body.

23. (currently amended) A method of preventing iron induced heart disease in ~~heavily transfused~~ transfusion dependent patients having an iron overload condition of the heart comprising administering to the patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof to chelate the iron stores in the heart in preference to the iron stores in less critical organs/tissue in the body.

24. (currently amended) A method of reversing iron induced heart disease in ~~heavily transfused~~ transfusion dependent patients having an iron overload condition of the heart comprising administering to the patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof to reduce the iron stores in the heart in preference to the iron stores in less critical organs/tissue in the body.

25. (currently amended) A method of treatment, prevention, or reversal of iron induced heart disease in a ~~heavily transfused~~ transfusion dependent patient having an iron overload condition of the heart comprising administering to the patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof for the direct reduction/removal of intracellular iron stores in the heart.

26. (currently amended) A method to prevent/treat/reverse the occurrence of iron-induced cardiac disease in ~~heavily transfused~~ transfusion dependent patients with an iron overload condition, comprising administering to said patient a therapeutically effective amount of deferiprone or a physiologically acceptable salt thereof, wherein deferiprone's efficacy is cardio preferential when compared with its ability to lower total iron stores in the body.

27-29 (cancelled)

30. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein deferiprone or a physiologically acceptable salt thereof is administered orally for preventing the risk of iron induced heart disease in patients having iron overload.

31. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein deferiprone or a physiologically acceptable salt thereof is administered orally for stabilizing the risk of iron induced heart disease in patients having iron overload.

32. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein deferiprone or a physiologically acceptable salt thereof is administered orally for reducing the risk of iron induced heart disease in patients having iron overload.

33. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein deferiprone or a physiologically acceptable salt thereof is present ~~is~~ in an oral dosage form with other excipients.

34. (cancelled)

35. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein the administration frequency to the patient of an amount of deferiprone or a physiologically acceptable salt thereof is daily and substantially in the range of up to 150mg per kilogram of body weight.

36. (cancelled)

37. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein the administration frequency to the patient of a dosage amount of deferiprone or a physiologically

acceptable salt thereof is daily and substantially in the range of up to 125 mg per kilogram of body weight.

38. (cancelled)

39. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein the administration frequency to the patient of a dosage amount of deferiprone or a physiologically acceptable salt thereof is daily and substantially in the range of 25mg to 75mg per kilogram of body weight.

40. (cancelled)

41. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein deferiprone is administered in a manner selected from the group of intravenously, transdermally, rectally, orally, bucally, or aurally.

42. (cancelled)

43. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein deferiprone is administered orally.

44. (cancelled)

45. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein deferiprone or a physiologically acceptable salt thereof is in a sustained release formulation.

46. (cancelled)

47. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein deferiprone has a cardio preferred/selective function when compared to desferrioxamine or other alternative chelating agents utilized in patients suffering iron overload.

48. (cancelled)

49. (currently amended) The method of claims 1, 2, 11, 12, 13, 22, 23, 24, 25 ~~and~~ or 26 wherein ~~deferiprone~~ desferrioxamine is administered in addition to ~~desferrioxamine~~ deferiprone.

50. (cancelled)

51. (cancelled)

52. (cancelled)

53. (cancelled)

54. (cancelled)

55. (cancelled)

56. (cancelled)

57. (cancelled)

58. (cancelled)

59. (cancelled)

60. (cancelled)

61. (cancelled)

62. (cancelled)

REMARKS

Claims 30-33, 35, 37, 39, 41, 43, 45, 47, 49, 55-58 and 60-62 now stand rejected under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must refer to other claims in the alternative only.

The method claims have been amended in accordance with Examiner's suggestion; namely "and" in the listing of the dependent claims has been changed to --or--. The composition claims have been cancelled without prejudice as to filing a continuation application.

Claims 11-13, 22-25, 30-33, 35, 27, 39, 41, 43, 45, 47 and 49 are allegedly rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for the treatment, prevention, stabilization or reversal of iron induced cardiac/heart disease, does not reasonably provide enablement for the treatment, prevention, stabilization or reversal of cardiac/heart disease in general. It is stated by the Examiner that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. These claims have therefore been amended to specify the disease as iron induced heart disease.

Claims 1, 2, 8-13, 18, 22-26, 30-33, 35, 37, 39, 41, 43, 45, 47, 49, 55-58, and 60-62 now stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "heavily transfused" has been replaced with the term "transfusion dependent" which term is supported in the disclosure as filed with PCT at page 23, line 25, page 35, line 27, page 38, line 23, and page 41, line 20 and line 29.

Claims 8, 9, 10, 18, 55-58 and 61 are rejected under U.S.C. 102(b) as being allegedly anticipated by any one of Olivieri et al., Hoffbrand et al. (Examiner cit. Ref. "U") or Hoffbrand (Examiner cit. Ref. "V"), each of record, for the reasons as set out in the previous Office Action. These claims have been cancelled without prejudice to filing a continuation application.

Claims 8, 9, 10, 18, 55-58 and 60-62 are rejected under 35 U.S.C. 103(a) as being unpatentable of Olivieri et al., Hoffbrand et al. (Examiner cit. Ref. "U") or Hoffbrand (Examiner cit. Ref. "V"), as above in view of Lai (U.S. Patent No. 5,922,761), each of record. Again, these claims have been cancelled without prejudice and will be pursued in a continuation application.

Further to discussions with the Examiner on December 1, 2004, it was agreed that if all the Section 112 objections and improper form objections were properly addressed that the method claims would be allowable. Applicants submit this has been done for the reasons set out above and it is assumed that this application will now proceed to allowance. The Examiner is thanked for his co-operation in this regard.

Attached for Examiner's review is an Information Disclosure Statement. The references cited in the Information Disclosure Statement are available on the enclosed CD, which is for reference purposes only. Please be advised that the references were cited in Applicant's corresponding PCT, European and Chinese patent application and these documents do not impact on patentability.

If the Examiner has any questions, he is requested to contact Neil H. Hughes at (905) 771-6414.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Registration No. 33,636
Agent for the Applicant

NHH/md
Enclosures

IN THE UNITED STATES PATENT OFFICE

Application Serial No. 10/311,814

Our Ref.: PC-1834033
CUSTOMER NO. 23607

Ivr fee only

Applicant:	Apotex Inc.	Agent:	Neil H. Hughes, P.Eng. c/o Ivor M. Hughes Barrister & Solicitor Patent & Trade Mark Agents Suite 200 175 Commerce Valley Dr. W. Thornhill, Ontario Canada L3T 7P6
Title:	A NEW USE FOR DEFERIPRONE		
Inventors:	Michael Spino and Antonio Piga		
Examiner:	Raymond J. Henley III		
Group Art Unit:	1614	**Due Date: December 8, 2004**	

RESPONSE TO OFFICIAL ACTION
OF SEPTEMBER 8, 2004

December 6, 2004

VIA COURIER

U.S. Patent and Trademark Office
220 20th Street South
Customer Window, Mail Stop Amendment
Crystal Plaza Two, Lobby, Room 1B03
Arlington VA 22202

Dear Sir:

This submission is in response to the outstanding Official Action dated September 8, 2004 and due for response December 8, 2004. Should any fee be required for this submission or if there is any deficiency or surplusage of fees required please obtain any such fees or deficiency or credit the surplusage to Deposit Account 08-3255 and advise Applicants' Agent.

Please enter the following submissions:

01/28/2005 FPATTERS 00000001 083255 10311814
01 FC:1202 4150.00 DA

Further to discussions with the Examiner on December 1, 2004, it was agreed that if all the Section 112 objections and improper form objections were properly addressed that the method claims would be allowable. Applicants submit this has been done for the reasons set out above and it is assumed that this application will now proceed to allowance. The Examiner is thanked for his co-operation in this regard.

Attached for Examiner's review is an Information Disclosure Statement. The references cited in the Information Disclosure Statement are available on the enclosed CD, which is for reference purposes only. Please be advised that the references were cited in Applicant's corresponding PCT, European and Chinese patent application and these documents do not impact on patentability.

If the Examiner has any questions, he is requested to contact Neil H. Hughes at (905) 771-6414.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Registration No. 33,636
Agent for the Applicant

NHH/md
Enclosures

PATENT APPLICATION FEE DETERMINATION RECORD
Effective October 1, 2003

Application or Docket Number: 10/311814

CLAIMS AS FILED - PART I

	(Column 1)	(Column 2)
TOTAL CLAIMS		
FOR	NUMBER FILED	NUMBER EXTRA
TOTAL CHARGEABLE CLAIMS	47 minus 20=	* 27
INDEPENDENT CLAIMS	14 minus 3 =	* 11
MULTIPLE DEPENDENT CLAIM PRESENT		☐

* If the difference in column 1 is less than zero, enter "0" in column 2

SMALL ENTITY TYPE ☐		OR	OTHER THAN SMALL ENTITY	
RATE	FEE		RATE	FEE
BASIC FEE	385.00	OR	BASIC FEE	770.00
X$ 9=		OR	X$18=	486
X43=		OR	X86=	924
+145=		OR	+290=	280
TOTAL		OR	TOTAL	

CLAIMS AS AMENDED - PART II

12/8/04

AMENDMENT A

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	* 130	Minus	** 47	= 83
Independent	* 10	Minus	*** 14	= —
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

SMALL ENTITY		OR	OTHER THAN SMALL ENTITY	
RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	~~X$18=~~ 18	1494 ~~4450~~
X43=		OR	X86=	
+145=		OR	+290=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	~~4450~~ 1494

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X43=		OR	X86=	
+145=		OR	+290=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

AMENDMENT C

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X43=		OR	X86=	
+145=		OR	+290=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20."
***If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3."
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

MULTIPLE DEPENDENT CLAIM FEE CALCULATION SHEET
(FOR USE WITH FORM PTO-875)

PATENT NO. 10/311814 | FILING DATE

APPLICANT(S)

CLAIMS

	AS FILED		AFTER 1st AMENDMENT		AFTER 2nd AMENDMENT											
	IND.	DEP.	IND.	DEP.	IND.	DEP.		IND.	DEP.	IND.	DEP.	IND.	DEP.		IND.	DEP.
1	1						51									
2	1						52									
3							53									
4							54									
5							55									
6							56									
7							57									
8							58									
9							59									
10							60									
11	1						61									
12	1						62									
13	1						63									
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22	1						72									
23	1						73									
24	1						74									
25	1						75									
26	1						76									
27							77									
28							78									
29							79									
30		10					80									
31		10					81									
32		10					82									
33		10					83									
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38							88									
39		10					89									
40							90									
41		10					91									
42							92									
43		10					93									
44							94									
45		10					95									
46							96									
47		10					97									
48							98									
49		10					99									
50							100									
TOTAL IND.							TOTAL IND.	10								
TOTAL DEP.							TOTAL DEP.	120								
TOTAL CLAIMS							TOTAL CLAIMS	130								

PTO-1360 (3-78)

*MAY BE USED FOR ADDITIONAL CLAIMS OR AMENDMENTS

U.S. DEPARTMENT of COMMERCE
Patent and Trademark Office

PATENT APPLICATION FEE DETERMINATION RECORD
Effective October 1, 2003

Application or Docket Number: 10/311814

CLAIMS AS FILED - PART I

	(Column 1)	(Column 2)
TOTAL CLAIMS		
FOR	NUMBER FILED	NUMBER EXTRA
TOTAL CHARGEABLE CLAIMS	47 minus 20=	* 27
INDEPENDENT CLAIMS	14 minus 3 =	* 11
MULTIPLE DEPENDENT CLAIM PRESENT		☐

* If the difference in column 1 is less than zero, enter "0" in column 2

SMALL ENTITY TYPE ☐		OR	OTHER THAN SMALL ENTITY	
RATE	FEE		RATE	FEE
BASIC FEE	385.00	OR	BASIC FEE	770.00
X$ 9=		OR	X$18=	486
X43=		OR	X86=	924
+145=		OR	+290=	280
TOTAL		OR	TOTAL	

CLAIMS AS AMENDED - PART II

12/8/04

AMENDMENT A

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	* 130	Minus	** 47	= 83
Independent	* 10	Minus	*** 14	= —
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

SMALL ENTITY		OR	OTHER THAN SMALL ENTITY		
RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE	
X$ 9=		OR	~~X$18=~~	~~4150~~	4150
X43=		OR	X86=		
+145=		OR	+290=		
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	~~4150~~	4150

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X43=		OR	X86=	
+145=		OR	+290=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

AMENDMENT C

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM				☐

RATE	ADDITIONAL FEE		RATE	ADDITIONAL FEE
X$ 9=		OR	X$18=	
X43=		OR	X86=	
+145=		OR	+290=	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20."
If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3."
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

IN THE UNITED STATES PATENT OFFICE

CUSTOMER NO. 23607

Application Serial No. 10/311,814 Our Ref: PC-1834033

Filing Date: April 4, 2003

Applicant: Apotex inc.

Agent: Neil H. Hughes
Suite 200
175 Commerce Valley
Drive West
Thornhill, Ontario
L3T 7P6, Canada

Title: A NEW USE FOR DEFERIPRONE

Inventors: Michael Spino and Antonio Spiga

Examiner: Raymond J. Henry III

Group Art Unit: 1614

No. of Pages of Response including this sheet: 8

DELIVERED TO FACSIMILE NO. (703) 872-9306

U.S. Patent and Trademark Office
220 20th Street South
Customer Window, Mail Stop Amendment
Crystal Plaza Two, Lobby, Room 1B03
Arlington, Virginia 22202

Dear Sir:

OFFICIAL COMMUNICATION

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the United States Patent Office Facsimile No. (703) 872-9306 on the date shown below, including:

1. Letter Dated February 17, 2005 with attachments

Signature: _____ Date: February 17, 2005

Neil H. Hughes
Registration No. 33,636
Agent for Applicant

Ivor M. Hughes
Barrister & Solicitor

Patent & Trade Mark Agents
Canada, United States

Barristers & Solicitors
Ivor M. Hughes
Rick Tuzi
Mark Ng

Patent Agents
Neil H. Hughes, P.Eng.
Marcelo K. Sarkis, P.Eng.
Wm. Kitt Sinden

Our Ref.: PC-1834033

February 17, 2005

VIA FACSIMILE: 703-308-5077

Director of the United States Patent and Trademark Office
Attention: Deposit Accounts
One Crystal Park
2011 Crystal Drive, Suite 307
Arlington, Virginia, 22202

Dear Sir:

Re: Response to Examination Report
Application Serial No. 10/311,814 filed on April 4, 2003
of Michael Spino and Antonio Spiga
for A NEW USE FOR DEFERIPRONE
Group Art Unit: 1614
Examiner: Raymond J. Henley III
Deposit Account No. 08-3255
Customer No. 23607

On December 7, 2004, we filed a response to an Examination Report issued by Examiner Raymond J. Henley III. In that response, we requested that any additional fees be deducted from our deposit account, No. 08-3255. We have since been advised that the amount of $4,150.00 was deducted from our deposit account. We contacted the Examiner for this application, Raymond J. Henley III, and he does not know why this amount was removed. As such, our understanding of patent practice, along with that of the Examiner, is that this amount which was deducted from the deposit account was done so in error and that we require the full amount along with the $25.00 service charge be refunded. The necessary filing and claim fees of $4888.00 were properly paid when the application was filed as demonstrated by the attached cover letter which accompanied the original national phase entry application. The most recent amendment did not add any claims to the case and therefore was clearly an error on the part of the United States Patent Office.

175 Commerce Valley Dr. W., Suite 200, Thornhill, Ontario, Canada L3T 7P6 Phone: 905 771-6414 Fax: 905 771-6420
website: www.ivormhughes.com email: mail@ivormhughes.com

We enclose a copy of our deposit account statement for January 2005, showing the transaction that occurred in error. If there are any questions please let me know.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Agent for Applicant
Registration No. 33,636

NHH:md
Enclosures

√cc: Raymond J. Henley III (via facsimile)

Ivor M. Hughes
Barrister & Solicitor
Patent & Trade Mark Agents
Canada, United States

Barristers & Solicitors
Ivor M. Hughes
Rick Tuzi
Patent Agents
Neil H. Hughes, P.Eng.
Marcelo K. Sarkis, P.Eng.
Wm. Kitz Sinden

Our Ref.: PT-1834033

December 19, 2002

VIA COURIER

COPY

The Commissioner of Patents
UNITED STATES PATENT OFFICE
2011 South Clark Place
Crystal Plaza 2, Room 1B03
Arlington, Virginia U.S.A. 22202

Dear Sir:

Re: National Phase Entry in the United States
based on International Application
Number PCT/CA01/00956 filed on June 28, 2001
of Apotex Inc.
for A NEW USE FOR DEFERIPONE
CUSTOMER NO. 23607
Due Date: December 30, 2002

Enclosed herewith please find the following documentation for filing with the Commissioner:

(a) Request Form PTO-1390 for National Entry into the United States of America;
(b) Informal combined Declaration for Patent Application and Power of Attorney document of Michael Spino and Antonio Piga;
(c) Copy of Published International Application Number WO02/02114 A1 published January 10, 2002, and International Search Report;
(d) Copy of Notification of Transmittal of the International Search Report;
(e) Copy of Notification of Transmittal of the International Preliminary Examination Report; and
(f) Preliminary Amendment attaching Exhibits A and B.

The Claims that stand in this U.S. National Phase Patent Application are **Claims 1, 2, 8 to 13, 18, 22 to 26, 30 to 33, 35, 37, 39, 41, 43, 45, 47, 49 and 51 to 62.**

Also, enclosed along with this material please find a cheque in the amount of **$4,888.00 US dollars** made payable to **"The Commissioner of Patents"**. This sum includes $924.00 for 11 independent claims over and above the three allowed per application, $2,664.00 for 148 claims over and above the twenty claims allowed per application, $280.00 for multiple dependent claims fee, $890.00 for the International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO, and $130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(e)). If there is any surplus or deficiency, the Commissioner is authorized to credit the surplus or take the deficit from Applicant's Agent's Deposit Account No. 08-3255 and advise Applicants' Agent.

Also enclosed herewith is a stamped, self-addressed verification card which we request that you kindly acknowledge and return to this office at the earliest opportunity.

We thank the Commissioner for his cooperation in this regard and look forward to receiving filing data in this matter.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Registration No. 33,636
Agent for Applicant

NHH:nse
Enclosures

FORM PTO-1390 (REV. 11-2002) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: PC-1834033

U.S. APPLICATION NO. (If known, see 37 CFR 1.5):

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/CA01/00956	28 June 2001 (28.06.01)	30 June 2000 (30.06.00)

TITLE OF INVENTION: A NEW USE FOR DEFERIPRONE

APPLICANT(S) FOR DO/EO/US: MICHAEL SPINO and ANTONIA PIGA

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [ ] The US has been elected (Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [X] is attached hereto (required only if not communicated by the International Bureau).
   b. [ ] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. [ ] is attached hereto.
   b. [ ] has been previously submitted under 35 U.S.C. 154(d)(4).
7. [X] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [X] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (Informal)
10. [ ] An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A preliminary amendment.
14. [ ] An Application Data Sheet under 37 CFR 1.76.
15. [ ] A substitute specification.
16. [ ] A power of attorney and/or change of address letter.
17. [ ] A computer-readable form of the sequence listing in accordance with PCT Rule 13*ter*.2 and 37 CFR 1.821 - 1.825.
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19. [ ] A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. [X] Other items or information: Acknowledgement Receipt Card

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO. PCT/CA01/00956	ATTORNEY'S DOCKET NUMBER PC-1834000

21. ☒ The following fees are submitted:

	CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO $1040.00		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO $890.00		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO $740.00		
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International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) $100.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 840.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$ 130.00	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	$	
Total claims	168 - 20 =	148	x $18.00	$ 2,664.00	
Independent claims	14 - 3 =	11	x $84.00	$ 924.00	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $280.00	$ 280.00	
TOTAL OF ABOVE CALCULATIONS =				$ 4,888.00	
☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.			+	$	
SUBTOTAL =				$ 4,888.00	
Processing fee of **$130.00** for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				$ ---	
TOTAL NATIONAL FEE =				$ 4,888.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +				$ ---	
TOTAL FEES ENCLOSED =				$ 4,888.00	
				Amount to be refunded:	$
				charged:	$

a. ☒ A check in the amount of $ 4,888.00 USD to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 08-3255. A duplicate copy of this sheet is enclosed.

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SEND ALL CORRESPONDENCE TO:

SIGNATURE

Neil H. Hughes, P.Eng.
NAME

33,636
REGISTRATION NUMBER

United States Patent and Trademark Office

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Deposit Account Statement

Requested Statement Month:	January 2005
Deposit Account Number:	083255
Name:	IVOR M. HUGHES, BARRISTER & SOLICITOR
Attention:	ESTE HUGHES
Address:	175 COMMERCE VALLEY DR WEST
City:	THORNHILL
State:	
Zip:	L3T 7P6

DATE	SEQ	POSTING REF TXT	ATTORNEY DOCKET NBR	FEE CODE	AMT	BAL
01/28	1	10311814	PC-1834033	1202	$4,150.00	$924.09
01/31	77	SERVICE CHARGE		9202	$25.00	$899.09

START BALANCE	SUM OF CHARGES	SUM OF REPLENISH	END BALANCE
$5,074.09	$4,175.00	$.00	$899.09

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1614

Ivor M. Hughes

Barrister & Solicitor

Patent & Trade Mark Agents
Canada, United States

Barristers & Solicitors
Ivor M. Hughes
Rick Tuzi
Mark Ng

Patent Agents
Neil H. Hughes, P.Eng.
Marcelo K. Sarkis, P.Eng.
Wm. Kitt Sinden
Samuel T. Tekie, P.Eng.

Our Ref.: PC-1834033

March 7, 2005

VIA COURIER
For Pick-Up at Local Federal Express Facility

Attention: Examiner Raymond J. Henley III

The United States Patent and Trademark Office
400 Dulany Street
Alexandria, Virginia
22313, U.S.A.

Dear Examiner Henley:

Re: United States Patent Application Serial No. 10/311,814
of Apotex Inc.
for A NEW USE FOR DEFERIPONE
Inventors: Michael Spino and Antonio Piga
Examiner: Raymond J. Henley III
Group Art Unit 1614
Customer No. 23607

In accordance with the recent telephone conversation with Examiner Henley, enclosed please find a supplementary CD with the references cited in the previously submitted Information Disclosure Statement dated December 6, 2004.

If the Examiner has any questions or comments, he is requested to contact Neil H. Hughes at (905) 771-6414.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Registration No. 33,636
Agent for Applicant

NHH/md
Enclosure

175 Commerce Valley Dr. W., Suite 200, Thornhill, Ontario, Canada L3T 7P6 Phone: 905 771-6414 Fax: 905 771-6420
website: www.ivormhughes.com email: mail@ivormhughes.com

ARTIFACT SHEET

Enter artifact number below. Artifact number is application number + artifact type code (see list below) + sequential letter (A, B, C …). The first artifact folder for an artifact type receives the letter A, the second B, etc.. Examples: 59123456PA, 59123456PB, 59123456ZA, 59123456ZB

#10311614UB

Indicate quantity of a single type of artifact received but not scanned. Create individual artifact folder/box and artifact number for each Artifact Type.

[1] CD(s) containing:
computer program listing [ ]
Doc Code: Computer Artifact Type Code: P

pages of specification and/or sequence listing and/or table [ ]
Doc Code: Artifact Artifact Type Code: S

content unspecified or combined [1]
Doc Code: Artifact Artifact Type Code: U

[ ] Stapled Set(s) Color Documents or B/W Photographs
Doc Code: Artifact Artifact Type Code: C

[ ] Microfilm(s)
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[ ] Video tape(s)
Doc Code: Artifact Artifact Type Code: V

[ ] Model(s)
Doc Code: Artifact Artifact Type Code: M

[ ] Bound Document(s)
Doc Code: Artifact Artifact Type Code: B

[ ] Confidential Information Disclosure Statement or Other Documents marked Proprietary, Trade Secrets, Subject to Protective Order, Material Submitted under MPEP 724.02, etc.
Doc Code: Artifact Artifact Type Code X

[ ] Other, description: _____
Doc Code: Artifact Artifact Type Code: Z

March 8, 2004

Please forward to Group Art Unit 1614

Amended Compact Discs

EXAMINER NOTE: THIS PAPER IS AN INTERNAL WORKSHEET ONLY. DO NOT ENCLOSE WITH ANY COMMUNICATION TO THE APPLICANT. ITS PURPOSE IS ONLY THAT OF AN AID IN HIGHLIGHTING A PARTICULAR PROBLEM IN A COMPACT DISC.

THE ATTACHED CD (COPY 1) HAS BEEN REVIEWED BY OIPE FOR COMPLIANCE WITH 37 CFR 1.52(E). ***Please match this CD with the application listed below.***

Date: 3/11/2005
Serial No./Control No. 10/311814
Reviewed By: K. SMITH Phone: 308 9210 ext. 118

☐ The compact discs are readable and acceptable.

☐ Copy 1 and Copy 2 of the compact discs are not the same.

☐ The compact discs are unreadable.

☑ The files on the compact discs are not in ASCII.

☐ The compact discs contain at least one virus.

☑ Other ONE CD SUBMITTED - NOT PROPER SUBJECT MATTER

IVOR M. HUGHES

BARRISTER & SOLICITOR
175 COMMERCE VALLEY DRIVE WEST
SUITE 200
THORNHILL, ONTARIO
CANADA
L3T 7P6
Facsimile (905) 771-6420

FACSIMILE COVER SHEET

DATE:	March 17, 2005
TO:	**Examiner Raymond J. Henley III**
COMPANY:	**United States Patent and Trademark Office**
FAX NO:	**1-703-872-9306**
FROM:	Neil H. Hughes
OUR REF:	**PC-1834033**
YOUR REF:	

NUMBER OF PAGES INCLUDING COVER PAGE: ___

MESSAGE:

Please see the attached letter and attachments.

Please notify the undersigned if you did not receive all pages as indicated:

Telephone: (905) 771-6414 Ask for: Morag Dowell

IVOR M. HUGHES
Barrister & Solicitor

Patent & Trade Mark Agents
Canada, United States

Ivor M. Hughes
Rick Tuzi
Mark Ng

Patent Agents
Neil H. Hughes, P.Eng.
Marcelo K. Sarkis, P.Eng.
Wm. Kitt Sinden
Samuel T. Telde, P.Eng.

Our Ref.: PC-1834033

March 17, 2005

VIA FACSIMILE 703-308-5077

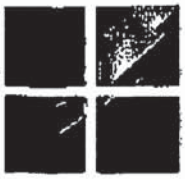
Mail Stop 16
Director of the United States Patent and Trademark Office
P.O. Box 1450
Arlington, Virginia, 22313-1450

Dear Sir:

Re: Response to Examination Report
Application Serial No. 10/311,814 filed on April 4, 2003
of Michael Spino and Antonio Spiga
for A NEW USE FOR DEFERIPRONE
Group Art Unit: 1614
Examiner: Raymond J. Henley III
Deposit Account No. 08-3255
Customer No. 23607

On December 7, 2004, we filed a response to an Examination Report issued by Examiner Raymond J. Henley III. In that response, we requested that any additional fees be deducted from our deposit account, No. 08-3255. We have since been advised that the amount of $4,150.00 was deducted from our deposit account. We contacted the Examiner for this application, Raymond J. Henley III, and he does not know why this amount was removed. As such, our understanding of patent practice, along with that of the Examiner, is that this amount which was deducted from the deposit account was done so in error and that we require the full amount along with the $25.00 service charge be refunded. The necessary filing and claim fees of $4888.00 were properly paid when the application was filed as demonstrated by the attached cover letter which accompanied the original national phase entry application. The most recent amendment did not add any claims to the case and therefore was clearly an error on the part of the United States Patent Office.

175 Commerce Valley Dr. W., Suite 200, Thornhill, Ontario, Canada L3T 7P6 Phone: 905 771-6414 Fax: 905 771-6420
website: www.ivormhughes.com email: mail@ivormhughes.com



We enclose a copy of our deposit account statement for January 2005, showing the transaction that occurred in error. If there are any questions please let me know.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Agent for Applicant
Registration No. 33,636

NHH:md
Enclosures

cc: Raymond J. Henley III (via facsimile)

Ivor M. Hughes
Barrister & Solicitor

Patent & Trade Mark Agents
Canada, United States

Ivor M. Hughes
Rick Turi

Patent Agents
Neil H. Hughes, P.Eng.
Marcelo K. Sarkis, P.Eng.
Wm. Kitt Sinden

Our Ref.: PT-1834033

December 19, 2002

COPY

VIA COURIER

The Commissioner of Patents
UNITED STATES PATENT OFFICE
2011 South Clark Place
Crystal Plaza 2, Room 1B03
Arlington, Virginia U.S.A. 22202

Dear Sir:

Re: National Phase Entry in the United States
based on International Application
Number PCT/CA01/00956 filed on June 28, 2001
of Apotex Inc.
for A NEW USE FOR DEFERIPONE
CUSTOMER NO. 23607
Due Date: December 30, 2002

Enclosed herewith please find the following documentation for filing with the Commissioner:

(a) Request Form PTO-1390 for National Entry into the United States of America;
(b) Informal combined Declaration for Patent Application and Power of Attorney document of Michael Spino and Antonio Piga;
(c) Copy of Published International Application Number WO02/02114 A1 published January 10, 2002, and International Search Report;
(d) Copy of Notification of Transmittal of the International Search Report;
(e) Copy of Notification of Transmittal of the International Preliminary Examination Report; and
(f) Preliminary Amendment attaching Exhibits A and B.

The Claims that stand in this U.S. National Phase Patent Application are **Claims 1, 2, 8 to 13, 18, 22 to 26, 30 to 33, 35, 37, 39, 41, 43, 45, 47, 49 and 51 to 62.**

175 Commerce Valley Dr. W., Suite 200, Thornhill, Ontario, Canada L3T 7P6 Phone: 905 771-6414 Fax: 905 771-6420
website: www.ivormhughes.com email: mail@ivormhughes.com

IVOR M. HUGHES

BARRISTER & SOLICITOR
175 COMMERCE VALLEY DRIVE WEST
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THORNHILL, ONTARIO
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L3T 7P6
Facsimile (905) 771-6420

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NUMBER OF PAGES INCLUDING COVER PAGE: 8

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IVOR M. HUGHES
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Patent & Trade Mark Agents
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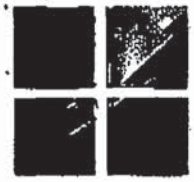

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Neil H. Hughes, P.Eng.
Agent for Applicant
Registration No. 33,636

NHH:md
Enclosures

cc: Raymond J. Henley III (via facsimile)

Ivor M. Hughes
Barrister & Solicitor
Patent & Trade Mark Agents
Canada, United States

Barristers & Solicitors
Ivor M. Hughes
Rick Tuzi
Patent Agents
Neil H. Hughes, P.Eng.
Marcelo K. Sarkis, P.Eng.
Wm. Kitt Sinden

Our Ref.: PT-1834033

December 19, 2002

COPY

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The Commissioner of Patents
UNITED STATES PATENT OFFICE
2011 South Clark Place
Crystal Plaza 2, Room 1B03
Arlington, Virginia U.S.A. 22202

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based on International Application
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CUSTOMER NO. 23607
Due Date: December 30, 2002

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175 Commerce Valley Dr. W., Suite 200, Thornhill, Ontario, Canada L3T 7P6 Phone: 905 771-6414 Fax: 905 771-6420
website: www.ivormhughes.com email: mail@ivormhughes.com

Also, enclosed along with this material please find a cheque in the amount of **$4,888.00 US dollars** made payable to **"The Commissioner of Patents"**. This sum includes $924.00 for 11 independent claims over and above the three allowed per application, $2,664.00 for 148 claims over and above the twenty claims allowed per application, $280.00 for multiple dependent claims fee, $890.00 for the International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO, and $130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(e)). If there is any surplus or deficiency, the Commissioner is authorized to credit the surplus or take the deficit from Applicant's Agent's Deposit Account No. 08-3255 and advise Applicants' Agent.

Also enclosed herewith is a stamped, self-addressed verification card which we request that you kindly acknowledge and return to this office at the earliest opportunity.

We thank the Commissioner for his cooperation in this regard and look forward to receiving filing data in this matter.

Respectfully submitted,

Neil H. Hughes, P.Eng.
Registration No. 33,636
Agent for Applicant

NHHmse
Enclosures

(REV. 11-2002)

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: PU 834033

U.S. APPLICATION NO. (If known, see 37 CFR 1.5):

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/CA01/00956	28 June 2001 (28.06.01)	30 June 2000 (30.06.00)

TITLE OF INVENTION: A NEW USE FOR DEFERIPRONE

APPLICANT(S) FOR DO/EO/US: MICHAEL SPINO and ANTONIA PIGA

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [ ] The US has been elected (Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [X] is attached hereto (required only if not communicated by the International Bureau).
   b. [ ] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. [ ] is attached hereto.
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   d. [ ] have not been made and will not be made.
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15. [ ] A substitute specification.
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18. [ ] A second copy of the published international application under 35 U.S.C. 154(d)(4).
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page 1 of 2

PCT/CA01/00956 PC-1834000

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International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO $890.00		
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ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 840.00	
Surcharge of $130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$ 130.00	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	$	
Total claims	168 - 20 =	148	x $18.00	$ 2,664.00	
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MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $280.00	$ 280.00	
TOTAL OF ABOVE CALCULATIONS =				$ 4,888.00	
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				Amount to be refunded:	$
				charged:	$

a. ☒ A check in the amount of $ 4,888.00 USD to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 08-3255. A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

SIGNATURE

Neil H. Hughes, P.Eng.
NAME

33,636
REGISTRATION NUMBER

United States Patent and Trademark Office

COPY

Deposit Account Statement

Requested Statement Month:	January 2005
Deposit Account Number:	083255
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DATE	SEQ	POSTING REF TXT	ATTORNEY DOCKET NBR	FEE CODE	AMT	BAL
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/311,814	04/04/2003	Michael Spino	PC-1834033	2281

23607 7590 03/29/2005

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CANADA

EXAMINER	
HENLEY III, RAYMOND J	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	10/311,814	SPINO ET AL.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,11-13,22-26,30-33,35,37,39,41,43,45,47 and 49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *12 and 13* is/are allowed.

6)☒ Claim(s) *1,2,11,22-26,30-33,35,37,39,41,43,45,47 and 49* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/8/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.